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PEDIATRICS

The Hygienic and Medical Treatment

OF

CHILDREN

BY

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FOUNDED UPON THE TEACHINGS OF THOMAS MORGAN ROTCH, M. D.

VOLUME II

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To

CLARENCE JOHN BLAKE, M.D., O.M. (Vienna), F.A.C.S.

Professor of Otology (Emeritus), Harvard University

THIS VOLUME IS INSCRIBED

As a tribute to his high professional attainments and to his unfailing
interest in the welfare of children, and in grateful
remembrance of many acts of kindness

BY THE AUTHOR

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CONTENTS

DIVISION VI

DISEASES DUE TO DISTURBANCES OF METABOLISM OR TO

CONSTITUTIONAL ANOMALIES	PAGE
Rachitis.....	2
Scorbutus.....	28
Purpura.....	41
Hemophilia.....	51
Acidosis.....	54
a. Cyclic Vomiting.....	59
b. Acid Intoxication.....	61
Diabetes Mellitus.....	73
Diabetes Insipidus.....	79
Spasmophilia.....	82
Pellagra.....	97

DIVISION VII

THE SPECIFIC INFECTIONS

Scarlet Fever.....	111
Measles.....	135
Rubella.....	151
Dukes' Disease.....	155
Varicella.....	157
Variola.....	164
Vaccinia.....	171
Diphtheria.....	176
Pertussis.....	214
Mumps.....	231
Influenza.....	237
Typhoid Fever.....	244
Malaria.....	260
Epidemic Cerebrospinal Meningitis.....	273
Poliomyeloencephalitis.....	295
Rheumatic Fever.....	319
Erysipelas.....	339
Tuberculosis.....	345
Syphilis.....	389

DIVISION VIII

DISEASES OF THE LARYNX, LUNGS AND PLEURA

I.—DISEASES OF THE LARYNX.....	422
Acute Laryngitis.....	423
Edema of the Larynx.....	429
Congenital Laryngeal Stridor.....	430

I.—DISEASES OF THE LARYNX— <i>Continued</i>	PAGE
Foreign Bodies in the Larynx.....	431
Papilloma of the Larynx.....	432
Chronic Laryngitis.....	433
II.—DISEASES OF THE LUNGS.....	434
Acute Bronchitis.....	434
Fibrinous Bronchitis.....	442
Chronic Bronchitis.....	442
Bronchopneumonia.....	444
a. Secondary Bronchopneumonia.....	446
b. Tuberculous Bronchopneumonia.....	460
c. Influenza Bronchopneumonia.....	467
d. Primary Pneumococcus Bronchopneumonia.....	470
e. Terminal Bronchopneumonia.....	471
f. Friedlander's Pneumonia.....	471
Lobar Pneumonia.....	472
Hypostatic Pneumonia.....	497
Gangrene and Abscess of the Lung.....	497
Atelectasis.....	498
Emphysema.....	498
Bronchiectasis.....	498
Asthma.....	500
III.—PLEURISY.....	508
Empyema.....	508
Serous Pleurisy.....	520
Fibrinous Pleurisy.....	525
Chronic Adhesive Pleurisy.....	527

LIST OF ILLUSTRATIONS

PLATE	COLORÉD PLATES	PAGE
III.—Infantile Scorbutus.....		29
VIII.—Scarlet Fever and Measles.....		118
IX.—Koplik's Spots.....		138
X.—Vaccination.....		174
XI.—Varicella, Syphilis, and Erysipelas.....		158
XII.—Diphtheria.....		182
154.—Facial Erysipelas.....		339

FIG.	FULL PAGE ILLUSTRATIONS	PAGE
118.—Rachitis, age six years.....		17
182.—Improvised crib tent for steam inhalations.....		427
185.—Secondary bronchopneumonia.....		451
186.—Secondary bronchopneumonia.....		453
188.—Secondary bronchopneumonia; roentgenogram.....		455
189.—Secondary bronchopneumonia; roentgenogram.....		455
190.—Bronchopneumonia; roentgenogram.....		455
191.—Tuberculous bronchopneumonia, subacute type.....		463
192.—Tuberculous bronchopneumonia; roentgenogram.....		464
193.—Tuberculous bronchopneumonia; roentgenogram.....		465
194.—Tuberculous bronchopneumonia; roentgenogram.....		466
201.—Lobar pneumonia; middle lobe.....		483
202.—Lobar pneumonia; roentgenogram.....		486

203.—Lobar pneumonia; roentgenogram.....	488
209.—Empyema, small effusion.....	515
210.—Empyema; roentgenogram.....	516
211.—Empyema; roentgenogram.....	517
212.—Empyema with pneumothorax; roentgenogram.....	519

FIG.	ILLUSTRATIONS IN THE TEXT	PAGE
109.—	Rachitic bone.....	3
110.—	Spindle-shaped rachitic bone.....	4
111.—	Rachitis with enlarged spleen.....	5
112.—	The rachitic head.....	11
113.—	Rachitic rosary.....	13
114.—	Position of the rachitic rosary.....	14
115.—	Rachitic kyphosis.....	14
116.—	Rachitic deformity of the spine and chest.....	15
117.—	Rickets.....	16
119.—	Rickets with deformity of the humeri.....	17
120.—	Roentgenogram of rickets.....	19
121.—	Section of scorbutic bone.....	31
122.—	Infantile scorbutus in an infant of nine months.....	33
123.—	Infantile scorbutus.....	34
124.—	Scorbutus; roentgenogram.....	35
125.—	Scorbutus; roentgenogram.....	36
126.—	Scorbutus; roentgenogram.....	36
127.—	Scorbutus; roentgenogram.....	37
128.—	Tetany.....	87
129.—	Pellagra.....	101
130.—	Pellagra.....	102
131.—	Pellagra in Italy.....	103
132.—	Pellagra.....	104
133.—	Pellagra in Italy.....	105
134.—	Varicella, third day.....	159
135.—	Apparatus for intubation.....	206
136.—	Intubation; beginning of the insertion of the tube.....	207
137.—	Intubation; completing the insertion of the tube.....	208
138.—	Intubation; withdrawing the tube.....	210
139.—	Pertussis during the paroxysm.....	219
140.—	Submaxillary mumps.....	234
141.—	Influenza bacilli in the sputum.....	239
142.—	Typhoidal ileo-colitis.....	246
143.—	Malaria with enlarged spleen.....	267
144.—	Malaria with enlarged spleen.....	268
145.—	Opisthotonos in meningitis.....	277
146.—	Chronic meningitis.....	278
147.—	Injection of serum into the spinal canal.....	286
148.—	Tapping the cerebral ventricles.....	289
149.—	Injection of serum into the cerebral ventricles.....	290
150.—	Position of insertion of the needle in tapping the cerebral ventricles.....	291
151.—	Poliomyeloencephalitis.....	303
152.—	Poliomyeloencephalitis.....	313
153.—	Rheumatic fever.....	326
155.—	Tuberculosis; primary lesion in the lungs.....	352
156.—	Tuberculosis; primary lesion in the lungs.....	353

FIG.	PAGE
157.—Miliary tuberculosis of the lungs.....	358
158.—Miliary tuberculosis of the lungs.....	359
159.—Tuberculous bronchopneumonia.....	360
160.—Tuberculous bronchopneumonia.....	361
161.—Tuberculous bronchopneumonia.....	362
162.—Tuberculous ulcer of the secum.....	363
163.—Tuberculous ulcers of the intestine.....	364
164.—Tuberculous ulceration of the intestine.....	365
165.—Tuberculous meningitis.....	366
166.—Tuberculous dactylitis.....	369
167.—Tuberculous dactylitis.....	370
168.—Examination for d'Espine's sign.....	372
169.—Chronic tuberculosis.....	373
170.—Tuberculous; primary stage.....	380
171.—Tuberculous; primary stage.....	381
172.—Tuberculosis bronchopneumonia.....	382
173.—Syphilitic maculae, ulcers, and bullae.....	399
174.—Syphilitic osteochondritis.....	400
175.—Syphilitic dactylitis.....	401
176.—Late manifestations of syphilis.....	404
177.—Syphilitic periostitis.....	405
178.—Syphilitic periostitis.....	406
179.—Hutchinson's teeth.....	407
180.—Technic of injecting neosalvarsan.....	417
181.—Congenital syphilis.....	419
183.—Lesion of secondary bronchopneumonia.....	448
184.—Lesion of secondary bronchopneumonia.....	449
187.—Acute bronchopneumonia.....	454
195.—Lobar pneumonia.....	480
196.—Lobar pneumonia.....	481
197.—Lobar pneumonia; upper lobe in front.....	482
198.—Lobar pneumonia; upper lobe behind.....	482
199.—Lobar pneumonia; lower lobe in front.....	483
200.—Lobar pneumonia; lower lobe behind.....	483
204.—Bronchiectasis.....	499
205.—Empyema from in front.....	513
206.—Empyema from behind.....	513
207.—Empyema, large effusion, front.....	514
208.—Empyema, large effusion, from behind.....	514

DIVISION VI

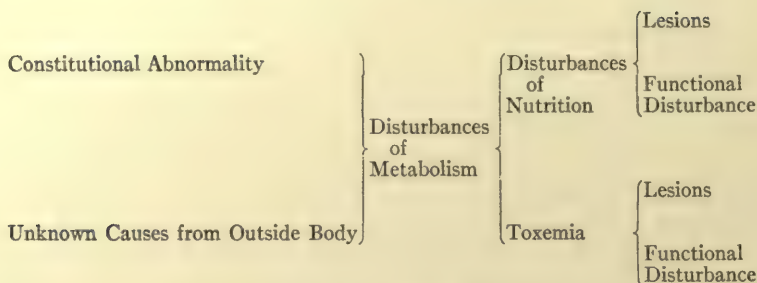
DISEASES DUE TO DISTURBANCES OF METABOLISM OR TO CONSTITU- TIONAL ANOMALIES

In this division are grouped a number of diseases of which the etiology is not definitely known. They are probably due to various abnormalities of the chemistry of the body, and consequently might be defined as constitutional diseases. The most probable cause of chemical abnormality is disturbance of metabolism, and this is the probable pathogenesis of the majority of the diseases of the group described in this division. In the case of hemophilia, however, the probability is that the disease is due to the direct inheritance of a constitutional abnormality, which involves the chemistry or structure of certain of the body tissues. In the other conditions, the cause of the chemical abnormality being unknown, it is attributed to disturbed metabolism. Whether or not an inherited constitutional abnormality plays a part, and if so, to what extent, and whether or not the chief part is played by causes acting from outside the body, and if so, to what extent, are unknown. Whatever the cause, these diseases present manifestations which strongly suggest that the tissue lesions, or functional disturbances produced, are due to disturbed metabolism.

Abnormality of metabolism produces two kinds of effects. The first effect is *disturbance of nutrition*. This may affect the body as a whole, or may affect certain particular tissues of the body. The result of disturbance of nutrition in childhood is an abnormality of development, with characteristic tissue lesions. The most conspicuous example of this effect of disturbed metabolism is the disease rachitis.

A second effect of an abnormality of metabolism is the formation of toxic products, resulting in a *toxemia*. The results of toxemia are again two-fold, one being the production of definite tissue lesions from the action of the poison, as in purpura, while the other result is a disturbance of function, as seen in spasmophilia.

The following scheme illustrates the probable pathogenesis of the diseases of this group:



RACHITIS

(Rickets)

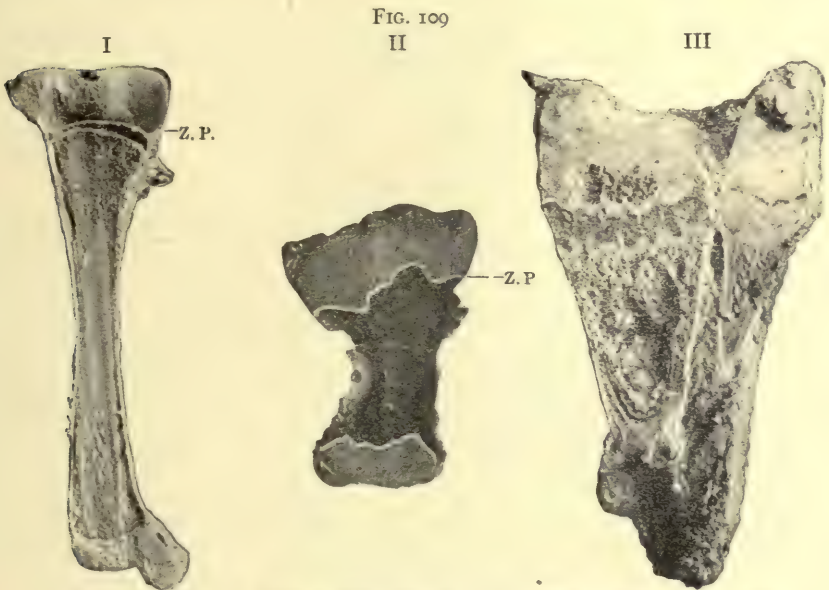
Rachitis, or rickets, is a constitutional disease, with definite anatomical lesions, which certainly represent a disturbance of nutrition. This in turn is almost certainly due to a disturbance of metabolism. All the organs and tissues are involved to some extent in the nutritional disturbance, but the principal lesions are in the bones. The nutritional disturbance produces the characteristic skeletal lesions by affecting the anatomical growth and development of the osseous tissue. As the lesions are the central feature of the disease, and as a knowledge of the tissue changes are essential to an understanding of the theories of the etiology of the disease, the pathological anatomy and chemistry of rickets will be described first.

PATHOLOGICAL ANATOMY. BONE LESIONS.—The pathological lesions of rachitis are represented chiefly in the bones, and occur during the period in which the normal processes of ossification are most active,—that is, during the first year and the first part of the second year of life.

The normal growth of bone depends upon four conditions: (a) multiplication of cartilaginous cells in definite lines, followed by (b) calcification of the intercellular spaces; (c) the formation of medullary spaces by the penetration of the blood vessels, with subsequent absorption of tissue; and (d) finally, the concentric deposition of calcium within the medullary spaces. The bones grow in length by the production of bone-tissue in the cartilage between the epiphysis and the diaphysis, and in thickness by the growth of bone from the inner layers of the periosteum. At the same time the medullary canal is enlarged in proportion to the growth of the bone by the absorption of its inner layer. These processes progress in definite order and in clearly defined zones.

In rachitis the chief microscopic features are the changes which occur in the zones of growth and the asymmetrical character of the proliferative processes. The cartilaginous and sub-periosteal cell-growth which produces ossification goes on with increased rapidity and in an irregular manner both between the epiphysis and the dia-

physis and beneath the periosteum. If we examine microscopically the region between the epiphysis and the diaphysis, usually called the zone of proliferation, we find that the cartilaginous cells are not regularly arranged in rows around a definite zone in advance of the ring of ossification, as in normal tissue, but there is an irregular heaping up of cartilaginous cells, sometimes in rows, sometimes not, covering an ill-defined irregular area. This zone of proliferation also, instead of being narrow and sharply defined, is quite lacking in uniformity. It presents a broad, reddish-gray appearance, with marked thickening and hyperemia. The medullary spaces are much more vascular than normal, and are so increased in area as to extend into



I. Normal bone: Z. P., zone of proliferation. II. Bone of a cretin: Z. P., zone of proliferation. III. Rachitic bone: Z. P., zone of proliferation

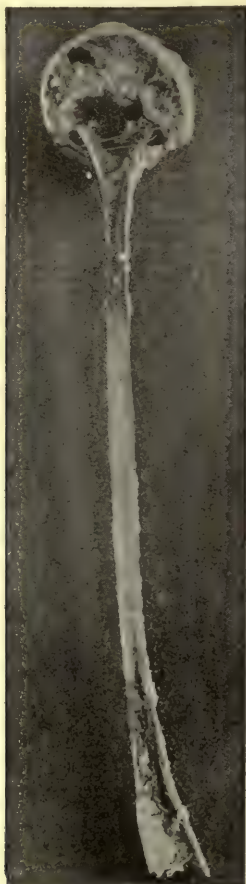
the zone of calcification, and sometimes through it. The deposit of calcium within these spaces is, however, either absent or very irregular, and is for the most part replaced by a soft, friable substance, consisting of a bone-tissue that is very lacking in lime-salts, with cells of various kinds embedded in a fibrillated ground-substance. This tissue is called "osteoid," and is similar to that formed by osteoblasts.

In the region of ossification (ends of diaphysis and epiphysis) there is microscopically a pronounced increase of blood-vessels and cartilage-cells, with lengthening of cell columns, and disturbance of calcification of the intercellular substance. Calcification, if present, may be isolated in the region of the proliferating cartilaginous cells,

or may be altogether absent over considerable areas. The subperiosteal layer of cells, which is normally thin and scarcely noticeable macroscopically, becomes hyperemic and thickened, with an appearance similar to that of spleen-pulp. Beneath this periosteum is also to be found the "osteoid" tissue seen in the zones of proliferation.

The medulla of the bone is more hyperemic even than normal. Its tissue is rich in cells, and like the fetal medulla, contains dilated

FIG. 110



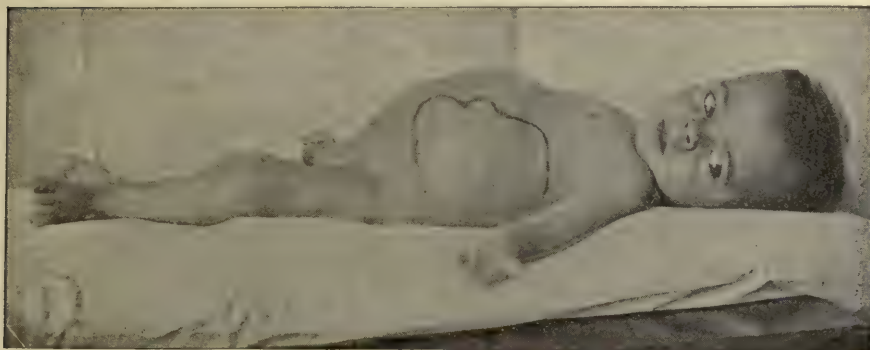
Spindle-shaped rachitic bone

vessels and fat. The intercellular substance may show mucoid degeneration or even be of fluid consistency. In such a condition it does not seem that lime is dissolved from the bone tissue by the blood, but it is the resorption of such bone *in toto* that is the important factor in the process. Resorption at the age at which rachitis occurs is normal. In rickets, rapid cases of softening certainly

show increased resorption. Ordinarily, with a resorption not greatly increased, the formation of fresh bone containing but little lime results in loss of strength. In the skull, in some places, absorption predominates (occiput); in other cases accretion of osteoid tissues (frontal and parietal eminences). Deficient bone-growth is the simple cause of enlarged fontanelles. In convalescence, lime is deposited in the previous limeless osteoid tissue, and the result is a thick and heavy bone. In fractures at this period callus-formation is intense and excessive.

The excessive proliferation of cells in the inner layers of the periosteum, the irregular calcification which occurs about them, and the absence of uniformity in the elaboration of the structure of the bone, produce an irregular, spongy bone-tissue instead of the compact lamellated tissue which is so necessary for the uniformity of the structure. The increased cell-growth between the epiphysis and the diaphysis produces the peculiar knobby swellings which are characteristic of rachitis. At the same time the medullary cavity

FIG. III



Male, 3 years old. Rachitis, with enlarged spleen

increases rapidly in size, and the inner layers of the bone become spongy. The result of these processes is to diminish the solidity of the bones so that they cannot resist the strain of the muscles or outside pressure, and consequently become bent and curved. After a time the rachitic process may stop and the bones may assume a more normal character. The porous bone-tissue becomes compact, and even unnaturally dense, so that in later childhood the rachitic bone is unusually hard, like ivory, a condition noticed by those who have to operate on these bones.

VISCERAL LESIONS; SPLEEN.—Investigations have shown that in cases of rachitis which come to autopsy, the spleen is invariably enlarged, with the exception of the cases of clearly pronounced atrophy, in which the spleen is of normal size and weight or below normal. A

second marked characteristic is the more or less significant thickening of the capsule and the increase in the consistency of the organ. The third peculiarity of the rachitic spleen is the anemia of the organ and the diminution in the number of Malpighian bodies, which in children are otherwise well developed, but in these conditions are hardly perceptible. On section, the spleen has a blood-red color, the trabeculae are clearly marked by interlacing threads, and on drawing the knife over the cut surface there remains upon the edge blood and pulp tissue. The characteristics described hold true in all cases of rachitis, and, in general, indicate approximately the intensity of the changes in the bones.

The microscopic appearances are those of an interstitial splenitis. Whether the inflammatory appearances are directly dependent upon the rachitis or are due to the complicating diseases which caused the death of the patient has never been definitely determined. The uniform appearances in all the cases irrespective of the cause of death, seem to give weight to the opinion that the lesions are directly connected with rachitis.

PATHOLOGICAL CHEMISTRY.—The rachitic bone and cartilage is abnormally poor in mineral constituents, that is to say, in calcium and phosphorus. The ash content of the ribs and spine may be reduced to from sixty to twenty per cent of the normal. Metabolism experiments up to the present time have only succeeded in establishing the fact that the diminished calcium content of the skeleton in rachitis is due to diminished calcium retention—a negative calcium balance, and that in the healing stage the calcium balance is reversed. This is no more than would be expected from the character of the condition. Up to the present time, metabolism experiments have been unable to throw further light on the pathological chemistry of rachitis.

ETIOLOGY. THE NATURE OF THE DISEASE.—The cause of rachitis is unknown. The disease is almost certainly a disturbance of nutrition, and the bony lesions being the most prominent feature of the disease, it has been assumed by many writers that rachitis represents a disturbance of the calcium metabolism. That the calcium balance is disturbed in rachitis is an undoubted fact, but this does not mean that the disturbance of calcium metabolism is the primary factor in the etiology of the disease. That rachitis is due to insufficient calcium in the food, or to insufficient absorption of calcium from the intestine, has never been proven, and is certainly contrary to the evidence. There remains the possibility that the disturbance involves the utilization of calcium by the tissues of the body. Sufficient calcium is absorbed, but not being used, is excreted again into the intestine. Under this theory, inability to use calcium

leads to the formation of lime-poor bone, which interferes with endochondral ossification. The other characteristics of the osseous lesions are considered secondary to this, the new cartilage being irregularly formed, while the medullary spaces, and an excessive number of blood vessels, project into the defective cartilage.

Another possibility is that the formation of defective bone tissue precedes and is the cause of the abnormality of the calcium metabolism. If this is the case, some other cause must be sought for the osseous lesions. The choice between these two theories must be a matter of opinion. I believe the weight of evidence to be against the theory that a specific disturbance of calcium metabolism is the primary factor. I believe that the calcium metabolism is disturbed only in this one respect, that the bony tissue is so affected by the disease that it is unable to seize and utilize the lime salts which are abundantly present for its use.

This does not, however, explain why the bony tissue is unable to utilize the lime salts. One theory, advanced by some writers, is that there is a special pathological peculiarity of the bony tissue which prevents ossification in rickets. Against this is the fact that rickets is not a disease limited to the bones, but affects all the organs and tissues of the body, which suffer in a manner which suggests disturbance of nutrition. If the bony tissues suffer with them, as a result of such disturbance, the effect in growing bone would quite naturally manifest itself by inability to carry on the most important function of such tissue, which is the storing of calcium. Moreover, histological and microchemical researches have given no evidence of any primary anatomical peculiarities of the bony tissue of the rachitic child, the lesions being suggestive of impaired nutrition.

The theory that a disturbance of metabolism in rickets causes an increased quantity of acid in the circulating body fluids, and that decalcification occurs through their influence, has not been supported, and is contrary to the preponderance of the evidence at hand.

From present knowledge, it can only be concluded that the disease rachitis represents a general disturbance of nutrition, in which all the tissues of the body suffer to some extent. Among them the bony tissue suffers, and the disturbance of nutrition so affects the growing bone, as to produce the characteristic osseous lesions of the disease. The effect of these lesions is impaired power of utilizing lime salts, and this leads to diminished calcium retention.

THEORIES AS TO ETIOLOGY.—In the voluminous literature of rickets will be found four principal theories as to the etiology of the disease. These are that the disease is caused, first, by an infection, second, by a disturbance of function of some of the ductless glands, third, by an unsuitable diet, and fourth, by bad hygienic surroundings.

The evidence in favor of the infectious nature of rachitis is very slight, and inconclusive. The weight of evidence points toward disturbance of metabolism as the most probable cause of the impaired nutrition.

The recent attempts to prove that some of the disturbances of metabolism are due to an impairment of the function of some of the ductless glands, such as the thyroid, parathyroid, thymus, and adrenals, have not been successful.

The two principal theories of the etiology of rachitis are the dietary, and the hygienic. According to the former, the disturbance of metabolism in rickets is caused by an improper diet. In favor of this theory are the facts that rickets is commoner in artificially-fed infants than in the breast-fed, and that it is also commoner when artificial feeding is badly conducted than when it is rationally conducted. Against it is the fact that the occurrence of rickets has never been conclusively associated with any particular dietary error, nor with any particular form of gastro-intestinal disturbance. Indeed, rickets is comparatively uncommon in the well-known gastro-intestinal diseases which lead to interference with growth, and atrophic infants are very infrequently severely rachitic. It is often seen in fat children, who have never had any digestive disturbance, and indeed, the disturbances of digestion in rickets seem to be usually secondary to the disease. The occurrence of rickets in fat children might partly be explained by diminution in their bodily activity.

It was formerly supposed that the most probable error in diet responsible for rickets was insufficient fat in the food. This was based on the statistical evidence obtained from the study of the previous diet of rachitic patients. The majority had been fed on foods high in carbohydrate, and low in fat, such as the various proprietary infant-foods. Such foods, however, are most commonly in use among the poorer members of society, where children are subjected to the worst errors of hygiene. Consequently no positive conclusion as to the influence of diet can be drawn from such statistics.

Metabolism studies on the effects of fat and carbohydrate on calcium metabolism, have suggested just the reverse theory as to the dietary error which causes rachitis. It has been shown that overfeeding with fat causes a negative calcium balance, while carbohydrate favors calcium retention. This phenomenon would only be of value in the etiology of rachitis, if the theory that the disease *is due* to a negative calcium balance were proven. It is possible, however, that overfeeding with fat may be a contributing cause.

No influence of diet on rachitis has yet been conclusively proven by any experimental method. We cannot, on the other hand, deny that the food, and its digestion, have any influence. How great a part the diet plays must be a matter of opinion. I believe that the

feeding certainly does not play the chief part in the etiology of rachitis. I believe, however, that improper feeding, and the nutritional disturbance which it causes, probably plays a contributory rôle in many disorders, among which is rachitis. This would explain the general frequency of rickets in the artificially-fed, without any relation to any particular dietary error. In breast-fed infants, rickets is seen at times, especially in babies with whom lactation is unduly prolonged, and also in Negro and Italian babies.

The fourth theory attributes rachitis to hygienic errors, and to faulty hygienic surroundings. This, I believe, is the view of the etiology of rachitis which is best supported by the evidence at hand. Rickets is commonest in the poorer classes; it is particularly common among the children of the proletariat of the larger cities. The housing conditions are of the first importance, and probably the most important factor is lack of fresh air. Confinement in small rooms, with overcrowding, gives lack of sufficient air space, and the absence of fresh air causes deficient oxygen intake. It is easily conceivable how serious disturbance of metabolism might follow such conditions. There is evidence also that among the unfavorable hygienic conditions contributing to rickets are lack of sufficient sunlight, and lack of sufficient bodily exercise. The probable influence on metabolism of both these factors is also obvious; lack of exercise, besides its direct influence on metabolism, would also lead to deficient oxygenation. Under this theory, rickets appears as a disease caused by the "domestication" incidental to civilization. All the conditions of civilization which differ from those of the natural life of the human animal, probably play some part. I believe this factor is far more important than are infections, or alimentary injuries or intoxications.

The evidence in favor of this view of the etiology of rachitis is both statistical and experimental. The remarkable investigation of Finlay in Glasgow is almost conclusive from the statistical standpoint. The frequency of rickets under crowded, unhygienic conditions, and its greater frequency of development in the winter and spring, when confinement to the house is common, are very significant. Also, the frequent development of rickets in animals confined in cages in zoological gardens, forms a very striking analogy. The only evidence against this theory is the infrequency of rickets among the inhabitants of polar countries, who live in close dwellings, deprived of sunlight for much of the year. Also, rickets is as common among the negroes of the South who live out of doors, as among our Northern negroes. This can be explained by the fact that another factor, that of race, is probably important in rickets. Such a factor must be assumed to explain the geographical distribution of the disease. The fact that rickets seen in breast-fed babies is common only among the Negroes and Italians, is further evidence of a racial

factor. There is some evidence also of the existence of a hereditary factor, a constitutional predisposition.

There is considerable experimental evidence on animals which supports the etiological importance of insufficient fresh air, exercise, and sunlight.

SUMMARY OF ETIOLOGY.—Rachitis is exclusively a disease of early life. It is only seen in infancy, the commonest period of its occurrence being that between the ages of six months and eighteen months. It may appear earlier, but is probably not congenital, the so-called congenital rickets representing a different disease (chondrodystrophy). It is a disturbance of nutrition, principally affecting the bones, causing definite lesions. It is accompanied by a marked disturbance of the calcium metabolism, but this is probably not the primary factor. Impaired nutrition of the bony tissue, which accompanies impaired nutrition of other tissues, causes the anomalies of calcium metabolism which are seen in the disease. The cause of the impairment of nutrition is probably a disturbance of metabolism, of which the nature is unknown.

The two chief causes of this are probably constitutional peculiarities, and injuries from without. Among the constitutional causes, the best established is the racial factor. There is some evidence in favor of a hereditary factor, but this probably is of very little importance. Of the external causes, the most important is probably faulty hygienic surroundings, including lack of fresh air, lack of exercise, and lack of sunlight. An unsuitable diet, various acute infections, and possibly chronic diseases, may act as contributory causes.

SYMPTOMS. CONSTITUTIONAL.—The symptoms of rachitis are those of a slowly developing constitutional disease. The early symptoms are the same as may occur in a number of diseases in which the nutrition is affected. The most common early symptoms are restlessness at night, profuse sweating, especially of the head, during sleep, and constipation. The appetite is impaired and capricious; the infants are fretful, the abdomen becomes prominent, and although they often grow fat they are anemic and their muscles are soft. The infants do not learn to walk as early as they should, their fontanelles do not close at the usual time; dentition is delayed and irregular, and soft areas appear in the cranial bones, especially in the occiput.

At this stage the characteristic tenderness of the body may occur, but many cases never present this symptom. This is usually due to a periosteal tenderness at the insertions of the muscles, and is sometimes confined to the bones. It is manifested only on trifling pressure, while at other times the muscles are tender and the gentlest effort to lift the child may cause him to shriek with pain. The

so-called paralysis of rachitis, which is an accompaniment of this stage, and, as a rule, precedes any marked osseous change, is generally brought to notice by the child's inability or disinclination to walk or stand. At other times it may be more severe and take the form of inability to use the arms as well as the legs.

After these general premonitory symptoms have continued for some time, the characteristic changes in the osseous system become prominent and are found in those parts of the bones which are in the most active stage of development. In cases beginning in earlier infancy, the skull undergoes the most marked changes.

FIG. 112



The rachitic head

HEAD.—The typical head of rachitis has a high, square forehead, with a decided prominence of the lateral parts of the frontal bones (frontal eminences), and sometimes there are also eminences on the parietal bones. The normal thickness of the bones is increased by means of a large amount of new periosteal soft growth between the periosteum and the bones. The head is somewhat lengthened and is usually larger in circumference than normal. The anterior fontanelle remains widely open, and may not ossify until the third year, or even later. The closure of the posterior fontanelle may be delayed in cases which develop rachitis very early in life. The sutures also remain open longer than normal, and in such cases may result in

leaving a depression in the course of the sagittal suture. Sometimes, however, a prominence is found instead of a depression. Flattening of the back and top of the head and asymmetry of the head may result from softening of the bones. The normal shape is usually regained when the disease is cured. The bones may be soft, porous, and hyperemic, while at their edges there may be rough, bony projections beneath the periosteum.

The name *craniotabes* is applied to an abnormal thinness of portions of the parietal and occipital bones, which are filled only with a fibrous membrane, and which yield to gentle pressure and give a sensation of crackling parchment. Upon recovery these areas show a thickened deposit of lime salts, and this condition of the bone may be only temporary, and the areas of thickening are often absorbed; but if there is much deposit under the periosteum it will sometimes remain, and where calcification takes place quickly, the thickened areas of the bone will remain unabsorbed throughout life. At times the jaw-bones are affected; the upper jaw is then found to spread behind, and to be pointed in front, while the lower jaw is flat in front and bent in at the sides, making an angle at the site of the canine teeth.

THORAX.—The rachitic thorax is narrow and is compressed laterally,—that is, there is a tendency to a flattening of the sides of the chest and to an increase of the antero-posterior diameter. The forces which produce deformities of the thorax are dependent on the muscular action on the soft bones by pulling, atmospheric pressure from without, and the pressure exerted on the bony structures by growing organs.

A transverse depression may also occur, starting at the junction of the ensiform cartilage with the sternum, extending laterally on the thorax, and corresponding to the insertion of the diaphragm. This is called Harrison's groove. The lower ribs may be elevated by the underlying distention caused by the prominent abdomen and the liver. Softening of the ribs is said to occur after the changes in the skull and before the changes in the extremities. In a typical rachitic thorax the clavicles are shorter and more curved than normal, and the clavicular deformities may be unilateral. Fractures of the clavicles in rachitis are not uncommon at the forward curve, and may possibly occur when the infant is being dressed.

When there is unusual lateral compression and narrowing of the thorax, the sternum is made to project forward, and this is called *pigeon-breast*, or *pectus carinatum*. The weakest part of the thorax is at the junction of the cartilages and ribs, and the sternum is thus naturally pushed forward. In another series of cases, in which the ribs are pushed together laterally and the sternum depressed, as where there is interference with the entrance into the lungs by adenoid

growths and enlarged tonsils, the condition of *funnel chest* is produced. Again, there may be greater compression on one side than on the other, with a resulting prominence or depression on one side of the sternum.

The costal cartilages are frequently enlarged at their junction with the ribs, and can be felt and often seen as a line of rounded prominences. These prominences are called the *rachitic rosary*, and, though most commonly occurring in the latter part of the first year, have also been met with in the early weeks of life. The rachitic rosary is the earliest of the physical signs of rachitis to develop, and is the most common abnormality in rachitis. It does not occur in normal children, and its presence justifies the diagnosis of rachitis.

FIG. 113



Inner surface of sternum, with cartilages and portions of ribs attached, showing rachitic rosary

As the pathological process is more pronounced in the lower ribs, especially the lower five, than the upper, the rosary is most distinct in the lower ribs.

SPINE.—Deformity of the spine is quite constant in rachitis and results mostly from muscular weakness, but the vertebrae may be affected by the rachitic process, and in cases of recovery may be found thickened. The most common deformity is *kyphosis*, which consists of a gradual bowing backward in the dorsal and lumbar regions.

The prominence of these vertebral spines is often quite sharp, and simulates Pott's disease, but the rachitic spine should be flexible to passive manipulation. *Scoliosis* (lateral curvature) and *lordosis* (forward curvature), are also common deformities occurring in rachitis.

FIG. 114



Position of the rachitic rosary

FIG. 115



Rachitic kyphosis. Female, 3 years old

EXTREMITIES.—Deformities of the long bones may arise in the epiphyses and in the shafts; the former show enlargement, the latter bending. Enlargement of the epiphyses appears especially at the wrists and at the anterior ends of the ribs; enlargement of the lower end of the radius and ulna is practically universal, and is second to the rosary in frequency of occurrence and in early time of appear-

FIG. 116



Rachitic deformity of the spine and chest

This particular deformity was caused by the fact that the patient had been cared for by an older child, who always held it with the same arm.

ance. Enlargement of the lower end of the tibia and fibula occurs next in frequency. The increase of the epiphyses at the wrists is greater than elsewhere. These enlargements do not involve the joints. In the deep-seated epiphyses, like the hip and the shoulder, the changes are not noticed so readily. The proliferating layer between the epiphyses and the bone may become so thick and softened that consequent deformity and separation of the epiphyses may occur, but such an event is uncommon. When fractures occur they are on the concave side of the bone. In rachitic deformity the curve of the forearm may be due to the pull of the muscles, and there may

be a special bend of the radius about the ulna, probably secondary to the anteroposterior curve. It prevents full supination. The humerus rarely bends. Fractures are not rare. Any considerable increase in the ankle epiphysis is rare. The curve of the femur is forward, and may involve only the anterior surface, so that there may be no curve on the posterior surface. Fractures may occur with excessive callus formation later. In the lower leg, fracture takes

FIG. 117



Rickets

place most often with anterior bowlegs, and the resulting callus is deeper than in the thigh. Fractures of the long bones, however, are uncommon, but their arrested development may cause permanent shortening. Bowing of the legs, knock-knee, and flat-foot, are all very common symptoms of rachitis. Coxa vara may be present. Localized rachitis, as of the legs, is possible and quite frequently met with in children with no symptoms of general rachitis.

Signs of previous rachitis are suggested by a caput quadratum with a thick skull, irregularity of the teeth, eversion of the lower edges of the thorax, pigeon-breast, pelvic deformity, deformities of the clavicles and extremities, and thickened epiphyses, which may



I

II

FIG. 118—Rachitis. Age, 6 years

persist, as thickened epiphyses in general are slow in disappearing and outlast the active process.

The existence of flat-foot in children over two years old should lead to an examination for knock-knee. The combination of these two conditions will in most cases be found to be dependent upon present or previously existing rachitis.

MUSCLES.—There is a weak and relaxed condition of the muscles and ligaments, but microscopically the muscles are only pale and their fibres infiltrated with fat, although in some cases there may be atrophy from disuse.

FIG. 119



Showing deformities of the humeri in a case of rachitis of an infant of 10 months, due to the habit, on the part of the mother, of lifting the child by the arms

NERVOUS SYSTEM.—The nervous system is in an exceedingly unstable and sensitive condition. Convulsions are quite common. Rachitic children have a marked tendency toward spasmophilia, with its characteristic symptoms of tetany and laryngospasm.

LUNGS.—Owing to deformities of the thoracic walls there is a tendency to atelectasis of portions of the lung from pressure, with surrounding areas of emphysema. There is also a great tendency to bronchitis and bronchopneumonia.

HEART.—The heart sometimes shows signs of mechanical irritation, represented by irregularity and caused by deformities of the thorax.

BLOOD.—Anemia is often seen in rachitis. The blood shows the characteristics of a secondary anemia.

LYMPH-NODES.—The lymph-nodes are very frequently found to be enlarged from simple hyperplasia.

STOMACH AND INTESTINES.—There is often, though not necessarily, functional disturbance of digestion. The symptoms vary very much and diarrhea and constipation alternate. The distended abdomen results from weakness of the muscles of the abdominal wall and of the intestine, and a resulting umbilical hernia is not rare. In like manner atonic constipation is common.

DIAGNOSIS.—The diagnosis of rachitis cannot be made by the premonitory symptoms, as the disease is so often the result of impaired nutrition arising from many causes, that it is difficult to determine when the rachitic symptoms begin. The differential diagnosis has to be made from a number of diseases in which the general nutrition of the child is profoundly disturbed, these diseases being especially represented by functional disorders connected with the gastro-enteric tract. When the pathological changes in the bones have progressed sufficiently for physical detection, and the disease is fully developed, the diagnosis is not difficult. In its early stages, therefore, the manifestations of rachitis may be so slight that the diagnosis must often be held in abeyance. The most significant signs are, in the order of frequency of occurrence, the rosary, the enlarged radial epiphyses, the rachitic head, delayed dentition, and the deformities of the chest. Prominence of the abdomen, relaxation of the ligaments, and enlargement of the spleen, are important confirmatory signs.

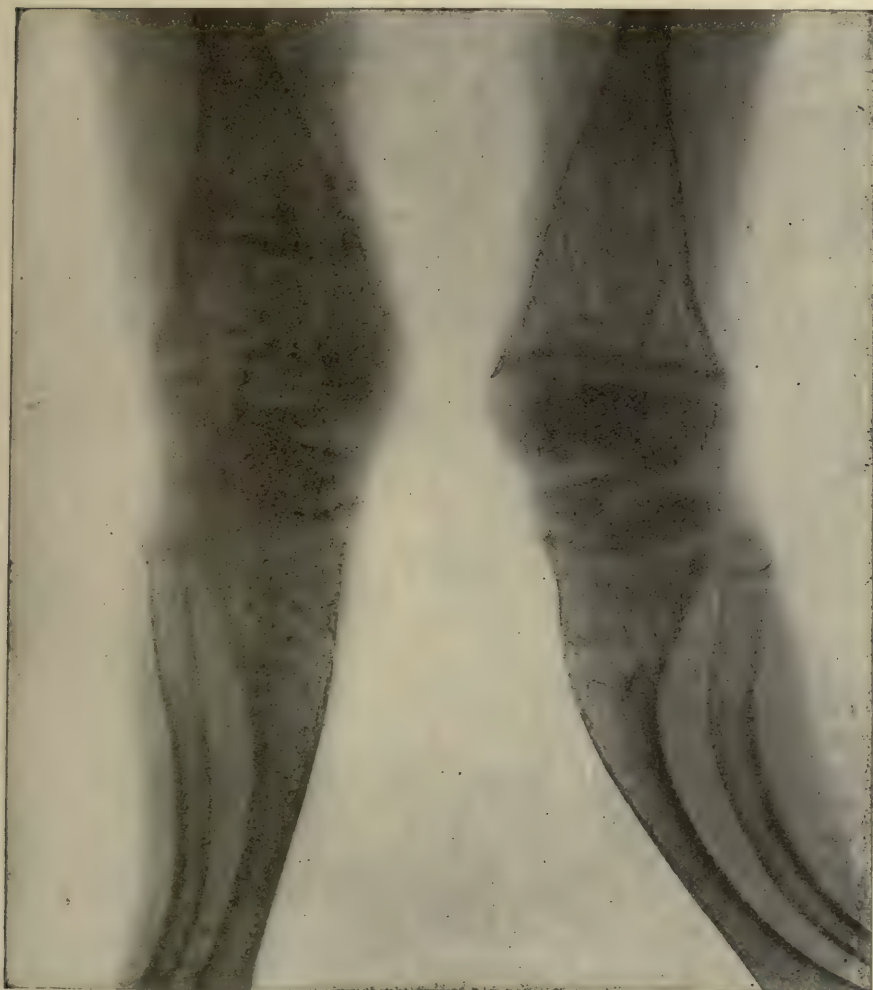
Examination with the roentgen ray is often of great value in the diagnosis of rachitis, and should be used in every case of doubt. The appearances of the bone structure as differentiated by means of the roentgen rays, from certain of the chronic conditions of childhood, may be summarized as follows: The characteristic curves of the long bones are easily apparent. There is great irregularity at the epiphyseal lines, with much hyperplasia of the osteoid tissue and hypertrophy of the epiphyseal cartilages. These pathological changes usually give the appearance of a great disproportion between the bony epiphysis and the epiphyseal ends of the diaphysis. The curves in the shafts of the bones are often sharp.

The differential diagnosis of rachitis is to be made from chondrodystrophy, scorbutus, rheumatism, osteomalacia, osteomyelitis, syphilis, paralysis of central origin, Pott's disease, and from the disability to use the limbs, due to simple weakness in infants who are not rachitic.

CHONDRODYSTROPHY, OR ACHONDROPLASIA, is distinguished from rachitis in the following characteristics: The trunk is normal, while the extremities are short and deformed. The head is large and the

bridge of the nose flattened. The enlargements at the ends of the long bones are due to overgrowth of the periosteum, instead of to changes in the epiphyseal cartilage, and the zone of proliferation is narrower than that in rachitis. A radiograph will usually bring out the differences in the pathology of the chondrodystrophy and all other lesions of the bones which resemble it. In this condition the epiphyseal lines, instead of being irregular, are straight, although much narrowed. The shafts of the bones are often thickened and

FIG. 120



Case of rachitis, the radiograph showing the marked deformity (knock-knee), the "zone of proliferation" at each epiphyseal line, as well as the marked rarefaction of the shadows cast by all the bones due in all probability to the deficiency in lime salts as well as to the change of function as to weight bearing.

stunted, while the apparent overgrowth of the bony epiphysis is so marked, that its shadow often appears to overlap that of the epiphyseal line.

SCORBUTUS is eliminated in the diagnosis by the presence of the various osseous lesions which have just been described as symptoms of rachitis, and by the absence of the characteristic features of scorbutus, represented by tenderness and swelling just above the joints, due to subperiosteal hemorrhages, and by stomatitis ulcerosa. The X-ray in scorbutus shows the raising of the periosteum by the characteristic subperiosteal hemorrhage. A "white line" at the epiphyseal zone of growth is considered characteristic by some authorities. The characteristic changes of rachitis are absent.

RHEUMATIC FEVER in its articular form would present such marked symptoms of acute tenderness, swelling, and pain in the joints, combined with a heightened temperature, that it could easily be distinguished from the general tenderness of the bones without much fever, together with the subacute or chronic course and the characteristic enlargement of the epiphyses in rachitis.

OSTEOMYELITIS.—The clinical symptoms of an acute infectious disease, with sudden onset, and represented by severe constitutional disturbance, heightened temperature, pain, localized tenderness, and rapid exhaustion, serve to distinguish osteomyelitis from the slow development and slight amount of fever met with in rachitis. In osteomyelitis, moreover, various foci of infection will appear in one or more bones with tenderness at these points and a tendency to suppuration which is not met with in rachitis. In roentgenograms the abnormal shadows are to be seen in the diaphysis, and are generally due to irregular necrotic areas, with or without sequestra. There is usually no thinning of the shadows of the involved bone or surrounding bones.

OSTEOMALACIA.—In very rare cases osteomalacia occurs in children, but it can seldom be differentiated from rachitis during life, except by X-ray examination. The lack of lime salts, as is shown by the "quality" of the shadow, is generally well-marked. The deformities of the bone-shafts are characterized by bendings rather than sharp curves.

HEREDITARY SYPHILIS.—The diagnosis of rachitis from hereditary syphilis is, as a rule, not difficult. While in rachitis the enlargement of the long bones is limited to the epiphyses, in syphilis it is not so limited, but involves the ends of the diaphyses. This enlargement is often accompanied by a condition which closely simulates a callus, and there is a distinct tendency to fracture in syphilis rather than to the bending which is common in rachitis. Lesions of the mouth and lips, and lesions of the skin are distinctive of syphilis.

CEREBRAL PARALYSIS AND POLIOMYELITIS.—In certain cases of rachitis, especially in the earlier stages, the so-called *paralysis of rachitis* occurs, and must be distinguished from paralysis of *central* origin, especially from poliomyelitis of the cord. The differential diagnosis must be made by the absence of the symptoms described under cerebral paralysis and poliomyelitis, and by an examination of the child in a recumbent posture, which in rachitis will show that the muscular movements are but little impaired, that the apparent inability to move the limbs and the disinclination to walk are caused by tenderness of the bones and muscular weakness, that the electrical reaction is normal, and that the reflexes are not affected. This pseudo-paralysis is certain to pass off if the child lives. Cases of rachitis which do not walk until late, on account either of muscular weakness or of tenderness, may resemble cases of organic nervous disease with true paralysis. The diagnosis must rest on the presence of the general signs of these nervous diseases.

POTT'S DISEASE.—When rachitis causes kyphosis of the spine, it may simulate Pott's disease very closely. A prominence may be present at the dorso-lumbar junction, which is a frequent seat of deformity in Pott's disease, and which, involving several vertebrae, may or may not be obliterated when the child lies on its face and is lifted by its feet from the table. The spine is held rigidly in severe cases, just as in Pott's disease, and the deformity may be angular rather than the usual gradual curve. The coexistence of enlarged epiphyses and other rachitic conditions makes it very probable that the affection is rachitic; but both diseases may coexist. The von Pirquet reaction is usually present in Pott's disease, and its absence is in favor of rachitis. In roentgenograms, abnormal shadows attributed to tuberculosis are to be seen most often involving the joints, while the appearances in the adjacent bones are characteristic.

In general, the age of the child, under eighteen months, the absence of much pain, and the existence of other signs establish the diagnosis of rachitis. Rachitis is, moreover, in children under two, much more common than Pott's disease. In doubtful cases the diagnosis can be made only after several examinations and a period of two or three weeks of recumbency, under which conditions the rachitic spine becomes somewhat more flexible. In doubtful cases time alone will establish the diagnosis.

WEAKNESS.—In certain infants who are not rachitic the power of walking is lost for variable periods, and is due to *weakness* following any disease, whether acute or chronic, which for a time may interfere with the infant's vitality. This condition is difficult to distinguish from rachitis, but must be differentiated by the absence of the other symptoms. Delay in learning to walk should lead us to

carefully examine for other symptoms of rachitis, as it is quite often one of the manifestations of this disease. An open fontanelle after the nineteenth or twentieth month suggests rachitis, and delayed dentition is also significant. If there are no teeth at the ninth or tenth month, the infant should be carefully examined for rachitis; at one year absence of teeth almost always indicates the disease.

Children with rachitis have weak muscles as well as weak bones, and the condition of such a child approaches that of one who stands and walks with the least expenditure of muscular force.

HYDROCEPHALUS.—The diagnosis between the rachitic head and the hydrocephalic is usually not difficult. The former is irregularly enlarged, flattened on top, square-looking, due to the prominence of the frontal bosses, and has a normally tense or depressed fontanelle. The latter is regularly enlarged and rounded, with prominent parietal bosses and a tense and bulging fontanelle.

PROGNOSIS.—The prognosis of rachitis is favorable, provided no complications arise. When left untreated the disease will, after more or less deformity has occurred, be arrested spontaneously, the pathological process in the bones will cease, and the bones will harden in their deformed condition. In these untreated cases the younger the child the more unfavorable is the prognosis as to permanent deformity. A spontaneous arrest of the disease may take place in any of its stages, but, as a rule, if the affection is pronounced, serious deformities are usually produced. Rachitic children are more liable to die than other children when they are attacked by such diseases as pneumonia or bronchitis. As a rule, the epiphyseal enlargements diminish with growth, but to a certain degree remain through life. In favorable cases the craniotabes, laryngismus stridulus, bronchitis, diarrhea and paralysis gradually pass away. Rarely death may occur in attacks of laryngospasm or convulsions.

When properly treated, the health of rachitic children improves steadily, and, unless the deformities which have occurred in the bones have advanced too far, complete recovery usually takes place by the third year. The arrest of the disease at an early stage is important. The persistent deformities are the curving of the long bones, the deformities of the spine, and the more advanced deformities of the chest.

TREATMENT. HYGIENIC.—The essential feature of the treatment of rachitis is removal of the cause. The treatment is therefore hygienic, and the earlier the treatment is begun, the better are the results. After the eighteenth month the harm has been done and the tendency is toward recovery on account of the changes in the mode of life of children at that age. Most of the cases seen in

private practice are comparatively mild and are often unrecognized until spontaneous recovery has already begun.

The degree to which faulty hygienic conditions can be corrected depends on the circumstances in the individual case. The ideal treatment only can be described, and this should be approached as closely as circumstances will permit. The essentials are fresh air, sunlight, and exercise. The rachitic child should be outdoors as much as possible. When indoors, he should be kept in well-aired rooms, which are not occupied by other children, or other persons. He should sleep in a room with well-opened windows. Exercise can only be attained with children who are able to walk. With babies unable to walk, the patient should be undressed daily in a warm room, and encouraged to roll and kick about. Massage is an extremely valuable substitute for exercise in babies unable to walk. Sponge baths in the morning, gradually made as cold as the vitality of the child will permit, are also valuable. In large cities it is advisable if possible, to send the patient to the country, because in cities, outdoor treatment is difficult to carry out, and sunshine difficult to obtain.

With the children whose domestic conditions prevent the full realization of proper hygienic surroundings, much can be done through social service organizations. Faulty hygienic conditions in the home can be remedied to a great extent. Frequent outdoor country excursions can sometimes be arranged, and the children can be kept as much as possible in the parks and open squares.

DIETETIC.—I do not believe that any specific modifications should be made in the diet of rachitic infants. There is no proven relation between diet and the disease to serve as a basis for such modification. Disturbances of digestion must, of course, be corrected. The evidence obtained by metabolism experiments of the influence of the various food elements on calcium metabolism is not, under present theories of etiology, sufficient to form a basis for treatment. As rachitis is most frequently seen in artificially fed infants, human milk is probably the best food for rachitic babies, as it is for babies in general. When artificial feeding is necessary, the next best food is cow's milk, and sufficient calcium to meet all requirements is present in all ordinary cow's milk modifications. In selecting the composition of the food, it must be borne in mind that the diet should be made as suitable as possible, the physician being guided by the general principles of infant feeding. When the diet best suited to the normal infant of the same age and development has to be modified, it is usually on account of the digestive peculiarities of the individual infant, and the changes which are made are designed to meet the clinical indications.

MEDICINAL.—No drug has been proven to have any influence on the essential pathology of rachitis. The discussion of the etiology showed the theoretical uselessness of giving calcium, and there is no convincing clinical evidence of its value. Cod liver oil and phosphorus, alone or in combination, have been widely recommended in the treatment of rachitis. In the case of cod liver oil there is no convincing evidence that it has any specific value. In view of certain experiments on the effect of fat on calcium metabolism, there is a possibility that cod liver oil might even do harm. I do not believe, however, that any specific harm from cod liver oil is established by these experiments. It provides a form of fat which is often easier of assimilation than cow's milk fat, and in any disturbance of nutrition, it is valuable as an adjunct to the diet. I do not think it should be used until the second year.

Phosphorus was first recommended by Kassowitz in the treatment of rachitis, and its effects have been the subject of much experimental and clinical investigation. It still holds first place in German therapeutics. The evidence is very conflicting, some investigations appearing to prove the value of phosphorus, and others exactly the reverse. While I believe the preponderance of evidence is against the value of phosphorus, I do not believe that it does any harm when properly used. The best preparation is phosphorated oil, one minim of which contains $\frac{1}{115}$ of a grain of phosphorus. The dose for infants is from one-half to one minim three times a day, after meals. It may be given in combination with one-half to one drachm of cod liver oil.

The only symptom in rachitis which often requires treatment is the anemia. The treatment is with iron, as in any secondary anemia. Profuse sweating may sometimes be relieved by atropine in doses of $\frac{1}{800}$ of a grain.

TREATMENT OF RACHITIC DEFORMITIES.—This is for the most part a matter for the orthopedist. For the deformities of the chest, breathing exercises and gymnastics are employed. The kyphosis can usually be overcome by postural treatment, massage, and exercises. The deformities of the extremities are either outgrown, or surgical measures are required.

PROBLEMS AND RESEARCH.—The problems connected with the study of rachitis have been suggested in the consideration of the etiology of the disease. At the present time, there is so much activity in experimental research devoted to the subject of rickets, and medical literature is so full of the discussion of the subject, that a summary of the most important recent investigations cannot fail to be of interest to the student. The chief reason for the activity of investigation on this disease, is the fact that research has given

to the investigator a definite measure, by which he can estimate the results of his experiments. The fact of a negative balance in the metabolism of the bone forming minerals—calcium and phosphorus—in the active stage of rachitis, has been proven beyond doubt. The great increase in calcium retention above the normal seen during convalescence has also been established. Consequently the experimental investigator is not dependent only upon the doubtful results of clinical observations, but can measure the results of his experiments by the effect on the retention of calcium.

One of the first steps in experimental research was the attempt to produce rickets in animals by using a food deficient in calcium. In many instances the animals became clinically rachitic, but the microscopic and chemical examination of their bones disclosed a condition differing from true rickets, to which condition Miwa and Stoeltzner gave the name of pseudorachitic osteoporosis.

Another series of investigations was devoted to the problem as to whether the lesions of human rickets are due to a primary calcium deficit in the food. This led to the establishment of the normal calcium requirement in infants, and also established the fact that in the cow's milk modifications used in artificial infant feeding, there is practically never a calcium deficit.

Investigators now turned their attention to the other possibility, that the lesions are due to deficient calcium absorption. The loss of calcium in such a case must be due to abnormal digestion. A great number of metabolism experiments showed that variations in the diet have an influence on calcium retention. In particular, a diet rich in fat increased calcium loss. None of the experiments have warranted the conclusion that decreased calcium absorption is responsible for the decreased retention. This led to the theory of Stoeltzner, outlined above, that sufficient calcium is absorbed, but that the bone, being for some reason unable to utilize it, the calcium is excreted into the intestine.

In connection with the problem of ultimate etiology, most of the theories are supported by clinical and statistical evidence, rather than by experimental evidence. Klose and Vogt, and Stoeltzner, support the theory of deficient internal secretion, particularly of the thymus. A rachitic condition has been produced experimentally in animals by ablation of the thymus. Mettenheimer, Matti, and Howland repeated the experiments and were unable to produce rickets in animals by removing the thymus. There is at present certainly no sure foundation for a thymic origin of rickets.

Some writers have expressed an opinion that the lesions of rickets suggest the action of a bacterial toxin, rather than that of a disturbance of nutrition. Marfan pointed out that probably all rachitic children have some focus of infection, and suggested the theory

of an intestinal autointoxication. Ribbert also advances the theory of a toxemia from bacteria, believing that all attempts to connect rickets with a special anomaly of metabolism, and all attempts to make it amenable to specific diet, have failed. The relation of rickets to improper feeding is explained by a lowering of the general resistance against infection. There has been some experimental work supporting the infectious theory. Koch injected the streptococcus longus into young animals, and an acute infection followed at once, gradually entailing a chronic disease of the bones which apparently was the same as rachitis in man. He believes, however, that domestication favors the development of the disease, as the dogs allowed to run about freely did not develop so marked a degree of disturbance of ossification as dogs kept in stalls. His experience confirms further the injurious influence of secondary infection after the process of normal ossification has once been upset by the acute infection. The ossification centres are left in a condition of lessened resistance, and an intercurrent whooping-cough, intestinal infection, or the like, adds fuel to the flame. He believes the injurious influence of infection alone, without calling on derangement of metabolism, is a sufficient explanation of the occurrence of rickets. In order to confirm Koch's evidence, further research is necessary, directed at showing whether other organisms beside the streptococcus longus can exert this malign influence upon ossification. Study of the pathological changes in the skeleton after acute infectious diseases in children might also throw some light upon the subject. The chief objection to conclusions drawn from experimental rickets in animals, is that the possible etiological influence of lack of fresh air, exercise, and sunlight, cannot be excluded in the conditions under which such experiments are usually carried out.

There has been considerable experimental work done in connection with the dietetic theory of the etiology of rickets, which attributes the disease to improper feeding. This work has been chiefly calcium and phosphorus metabolism experiments, showing the effects of various diets upon the retention of those minerals. An undoubted influence of diet upon calcium and phosphorus metabolism has been demonstrated, but the result still lacks the links necessary to positively connect it with rachitis. The production of experimental rickets in animals by any specific method of feeding, has not been conclusively attained. Orgler's conclusions are perhaps the most noteworthy; he believes that there are two important conditions which regulate calcium assimilation, (1) the ability of the tissue to assimilate it, which depends on the intermediary metabolism concerning which nothing is known; and (2) the composition of the food.

In favor of the "hygienic" or "domestication" theory of the

etiology of rickets, in which the factors of overcrowding, insufficient air, lack of exercise, and deprivation of sunlight are considered essential the evidence is mainly statistical. While statistical evidence is usually of less value than experimental evidence, some of the reports, such as Findlay's statistical investigation of from 400 to 500 rachitic children in the city of Glasgow, are very convincing. In pursuing this study Findlay investigated the possible rôle of the following factors: (1) the length of the time the child was breast-fed; (2) the order of the child in the family; (3) the condition of the bowels previous to the onset of the trouble; (4) the amount of air space in the house allowed to the child; (5) the number of stairs to be mounted to reach the house, and finally (6) whether or not the child has been taken much out doors. There is also experimental evidence in favor of the hygienic theory. Kochmann and Petzsch have recently demonstrated experimentally that under otherwise normal conditions of life, lack of exercise prevents the retention of a sufficient amount of calcium. Raczynski has shown also that less calcium was retained in dogs deprived of sunlight.

A great quantity of experimental work has been done on the therapeutic value of the "phosphorlebertran," the combination of phosphorus with cod liver oil so widely used in Germany. Most prominent is the work of Schabad. All these investigations consist in metabolism experiments on rachitic children, in which was studied the influence of phosphorus alone, cod liver oil alone, the two combined, and other oils substituted for cod liver oil, upon the metabolism of calcium, phosphorus, nitrogen, fat, and other salts. The results of all this work have been very contradictory. Kissel found in animal experiments, that phosphorus had no influence on the osseous tissue. Birk and Schabad both concluded that while phosphorus has no beneficial action in healthy children, the combination of phosphorus and cod liver oil increases the retention of phosphorus and calcium in rachitic children. Later work showed apparently that the effects are variable, or that there was no influence at all in acute rickets. The most recent investigation is a very elaborate series of metabolism experiments by Schloss of Berlin, which were carried out in rachitic breast-fed infants in order to exclude the possible disturbing influence of diet. He found that the phosphorlebertran had no favorable influence on the rachitic metabolism, except when combined with calcium acetate, when the favorable effects on the calcium and phosphorus balance were very striking. It does not seem probable that all this work is likely to lead to any very positive results, but it is probable that the literature of the next few years will continue to be largely occupied by the results of metabolism and animal experiments.

SCORBUTUS

(Scurvy) (Barlow's Disease) (Die Möller-Barlowsche Krankheit)

Scorbutus is a constitutional disease closely associated with nutrition. The identity of the disease as it occurs in infancy with the scurvy of adults was not recognized in the older writings, and infantile scurvy was usually described as acute rickets. Our modern knowledge of the pathology of infantile scurvy is based on the observations of Barlow and Cheadle.

Infantile scorbutus is a hemorrhagic disease. The disease is primarily characterized by a tendency to hemorrhage, especially under the periosteum of the bones, into the gums, into the skin, and from various mucous membranes. Anemia and cachexia are secondary manifestations.

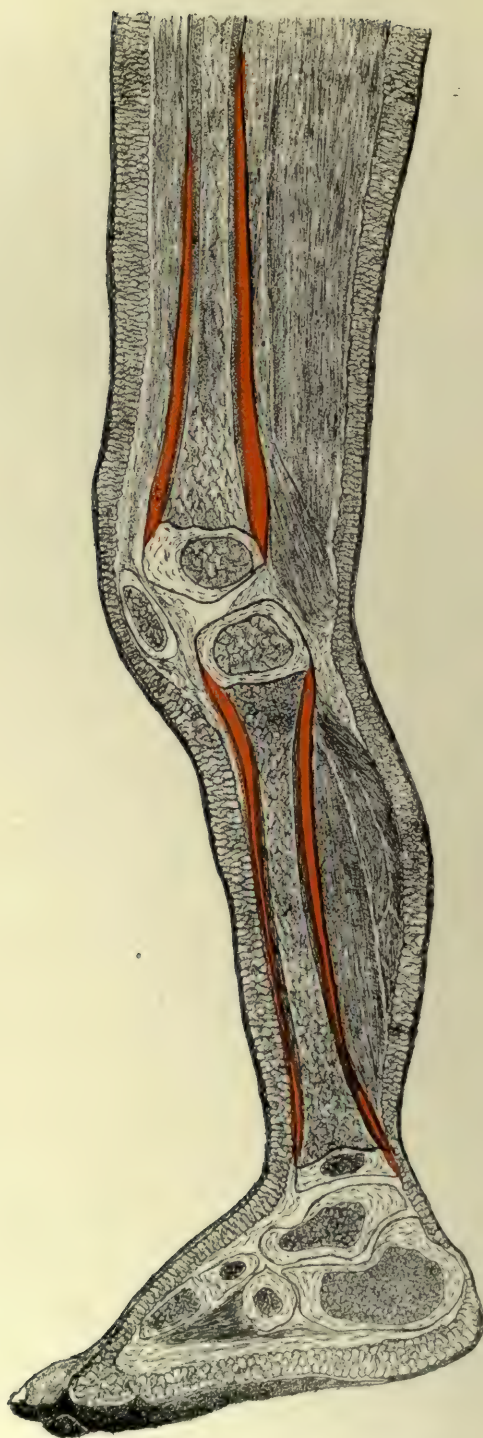
ETIOLOGY.—The exact cause of scurvy is unknown. A number of facts based mainly on clinical observation, though partly on experimentation, are known as to the etiology of the disease.

Leaving aside the scurvy of adults, such as develops among the members of polar expeditions, scurvy is exclusively a disease of infancy, and is never seen in older children. It occurs most frequently between the ages of six months and fifteen months, though a few cases are seen earlier than six months. It is probable that the presence in the infant at birth of antiscorbutic substances accounts for the time of appearance of the disease, as the disease frequently develops at seven to ten months after feeding with the same diet from the time of birth. The period when the disease occurs is just when antiscorbutic substances might be expected to be exhausted, and just before they are renewed by a more varied diet.

Clinical observations suggest the following conclusions: First, the hygienic surroundings have no influence whatever in the production of scurvy. The disease is fully as common, if not more common, in the infants of well-to-do parents brought up under the best hygienic conditions. Second, there is not the slightest evidence that previous disease, either acute or chronic, has any influence as a predisposing cause, and there is no evidence of any association with bacterial infection. Third, there is no evidence that digestive disturbance is a predisposing cause. Fourth, clinical experience shows a distinct association between the occurrence of scurvy and the diet, and a very rapid recovery under exclusively dietetic treatment.

It therefore appears that scurvy is due to a dietetic error. Furthermore, clinical experience suggests that the error in the diet is prolonged, and that it is not of such a character as to disturb the function of digestion. This strongly suggests that the improper feature

PLATE III



Vertical section of leg in a case of infantile scorbutus. The red areas around the femur and tibia represent subperiosteal hemorrhages. (Specimen preserved in the Museum of the College of Physicians and Surgeons, New York.)

of the diet is not an excess of any food element, but rather the *lack of some essential element in the food*.

Scurvy is very much more common in artificially-fed infants than in breast-fed. It is seen, however, in breast-fed infants. The occasional occurrence of the disease in breast-fed infants, and the fact that it does not always occur in the artificially-fed, proves that the disease is not due to the lack of some element found only in human milk, and the frequency of the occurrence of scurvy in the artificially-fed is probably to be explained by the great variety of artificial food-combinations in use, which allows a greater opportunity for the lack of a sufficient amount of some essential antiscorbutic substance. The analysis of a series of cases of scorbutus with reference to the diet has been undertaken from time to time, notably by a committee of the American Pediatric Society in 1898, and since then by various observers. These studies have shown no definite and constant relation between scurvy and any particular dietary error, which would point to the particular element which is lacking, but they are nevertheless very suggestive.

There is no suggestion of any connection between scurvy and a lack of fat, carbohydrate, protein, or any mineral salt. Scurvy occurs most frequently in infants fed for a long time on proprietary foods prepared without milk. It occurs next in frequency in infants fed on foods containing milk, but which have been prepared by the use of heat. This suggests that the substance of which the lack causes scurvy, is contained in milk, and that it is unfavorably influenced by heat.

The statistical evidence as to whether the heating of milk is a factor in the production of infantile scurvy is conflicting and inconclusive. In general, the weight of evidence points toward the conclusion that heating is an important etiological factor. In most series, the statistics show that the larger proportion of cases occur in babies fed on heated milk. Nevertheless, while scurvy occurs more frequently in babies taking condensed milk, or boiled milk, or pasteurized milk, it also occurs in breast-fed babies and in babies fed on raw milk. This suggests that the heating of milk, even if it is of importance, is not the sole etiological factor. The fact that scorbutus does not always appear when babies are fed on heated milk, suggests that the antiscorbutic elements are not all completely destroyed by heat. There is evidence that the degree of heat, the length of the heating, and the time which elapses after heating before use, all have an influence. Several series show that more cases are seen in babies fed on milk sterilized, boiled, or scalded, than on milk simply pasteurized. Plantanza observed that scurvy developed more frequently with heated milk, but not when fresh milk was heated and used at once.

There have been some animal experiments on the effects of raw and heated milk, but they are few and inconclusive.

If heat is a factor, we must assume that it may wholly or partially destroy the antiscorbutic element or elements in the milk, and thus produce a deficiency. The occurrence of scurvy in breast-fed babies, and in babies fed on raw milk, can be explained on the ground of a deficiency of the same essential element from some other cause. In breast-fed infants such deficiency must be due to an anomaly of lactation. It is possible that dietetic error in the mother may account for the deficiency of her milk, but there is as yet little evidence in support of such a theory. In artificial feeding, the methods of cow's milk modification consist largely in dilution, and it is easily conceivable how a deficiency of some essential element can thus be brought about. In my own clinical experience, scurvy has occurred in a number of babies fed on raw milk, but in every case, the digestive peculiarities of the baby required a particularly dilute food, or the over-anxiety of a nurse or mother caused her to dilute the food without sufficient reason. I believe that *too dilute a cow's milk modification is an important etiological factor* in the occurrence of scurvy, and that dilution as well as heat may cause a deficiency of the essential antiscorbutic substance.

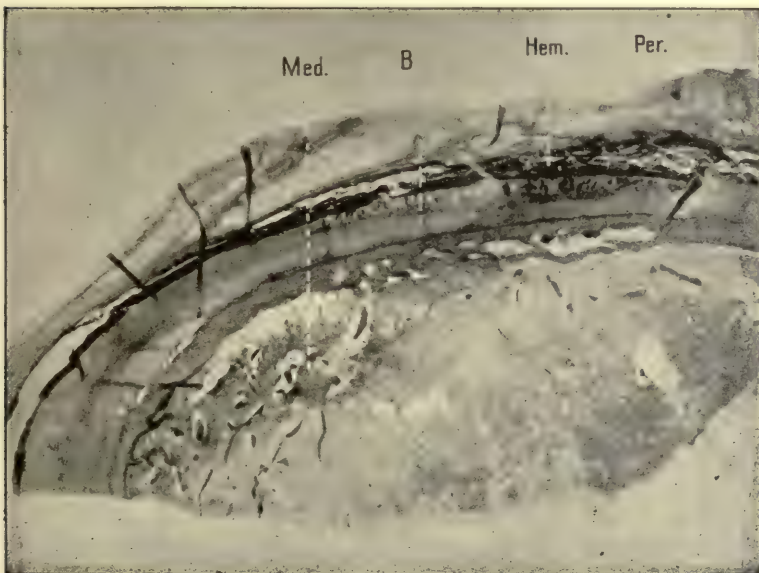
The nature of the essential element or antiscorbutic substance, the lack of which probably causes scurvy, remains unknown. There have been a number of investigations on animals, in which scorbutus has been produced experimentally. They have shown conclusively that scurvy is not due to simple starvation, nor to the prolonged use of a single article of food. They strongly support, however, the theory of the dietetic origin of the disease, and also strongly suggest that when scurvy develops as the result of the continuous use of any single food, it is *not the presence in the food, but the absence in the food*, of some substance which causes the disease. These experiments also suggest that this substance can be partially or wholly destroyed in various foods by heating or drying. They throw no light on whether there are one or more antiscorbutic substances, or on their nature.

One factor remains to be considered. Scurvy does not develop in all babies, in which the same prolonged error in diet is present. This suggests that there must be a constitutional predisposition which renders the production of scurvy easier in some individual babies. Such a factor probably plays some part. Hess' recent investigation suggests a connection between a predisposition to scurvy and the so-called "exudative diathesis" of Czerny. This has not yet been confirmed by other writers.

PATHOLOGICAL ANATOMY.—The most striking gross lesion

is hemorrhage, and the most characteristic site of hemorrhage is under the periosteum of the bones. The subperiosteal hemorrhage may affect any of the bones of the body, but the most commonly affected are the long bones of the lower extremities. These hemorrhages are often very extensive, and may run the entire length of the bone. The periosteum in severe cases may be entirely separated from the shaft by the extravasated blood, remaining attached only to the epiphyses. The epiphyses may also be separated from the shaft. While subperiosteal hemorrhage is so common as to be practically constant, hemorrhages may occur in other parts of the body. The most common location is in the gums of infants having teeth. Hemorrhage may also occur into the skin, between the muscles, and into the cellular tissue around the joints, although the joints them-

FIG. 121



Section of scorbutic bone. Med., medulla; B, bone; Hem., hemorrhage; Per., periosteum

selves are usually normal. Hemorrhage may also occur in any of the internal organs; hematuria is the commonest form. Hemorrhage into the cellular tissue of the orbit, pushing the eye forward, is seen at times, as are also small hemorrhages beneath the pleura, pericardium, or peritoneum.

Microscopic changes are confined mainly to the bones. The lesions differ from that of rickets in that it is the tissue of the bone marrow which is mainly affected. The myeloid tissue proper does not develop, so that the bone marrow is poor in cellular elements. The connective or supporting tissue increases at the expense of the

myeloid cells and blood vessels, and forms a homogeneous ground substance which contains numerous stellate and spindle-shaped cells. These changes are most marked at the ends of the diaphysis of the long bones, and at the ends of the ribs. As a result, the function of the osteoblasts is interfered with, calcification is diminished, and the cortex of the bone becomes thinner and more brittle. The density of the bone is particularly diminished near the epiphyseal line, but there is also an area of increased density at this point, forming the "white line" seen in roentgenograms.

The weight of American and English opinion differs from that of many European authorities on the interpretation of the lesions of scorbutus. Most European authorities regard the changes in the bone marrow as primary, leading to interference with the hemato-poietic function of the tissue, and consider that this leads to progressive anemia and the "hemorrhagic diathesis." This view regards the hemorrhage as a secondary lesion. American opinion regards the hemorrhage as an early and essential effect of the cause which produces the disease. Scurvy is thus essentially a hemorrhagic disease, and studies on the blood suggest that the lesion is not due to any change in the blood, but to a change in the blood vessels. Under this view, the same cause produces changes in both the bone marrow and the blood vessels.

SYMPTOMS.—The symptoms of infantile scorbutus are those of a slow and progressive cachexia. The infants become pale, and show more or less gastro-enteric disturbance of a functional type. Profuse sweating, especially about the head, at times slight feverish attacks, and lessened appetite, are among the early symptoms. The temperature may be from time to time slightly raised, but not significantly so. The first symptom, however, which especially attracts the attention is a sensitive condition of the bones. The infant cries when the affected parts are touched. It does not seem to suffer pain when it is allowed to remain quiet, but as the disease advances the expression of its face indicates the fear of being handled. At this stage, pressure over the legs or thighs will usually elicit signs of tenderness.

As the disease progresses, more marked symptoms develop. Swellings of the limbs, usually of the diaphyses just near the epiphyses, appear. These swellings are most common and most prominent in the legs, but may also appear in the bones of the forearm. They are usually pyriform and symmetrical in shape, the skin over the swelling being more or less *tense, but not fluctuating*. There is commonly marked tenderness on pressure, but, as a rule, no especial heat of the affected part. The pain and swelling do not seem to be in the joint, but in the diaphysis and epiphysis.

The symptom second in frequency to tenderness and swelling over the bones of the legs, is hemorrhage into the gums. This is only seen when an infant has teeth, or when the teeth are just beneath the surface. The mucous membrane of the gums at the free margin of the teeth becomes reddened and soon begins to swell. The normal curve of the gum becomes almost a straight line and covers

FIG. 122



Infantile scorbutus in an infant of 9 months, showing extreme sub-periosteal hemorrhages of both femora, with slight affection of the lower ends of both tibiae

the lower part of the teeth. The gums in the space between the teeth remain unaltered at first. The mucous membrane then begins to change in color and becomes purplish. Extreme congestion and softening of the tissues allow hemorrhage to take place from the slightest pressure. Even when there are no teeth, when a tooth

is pressing on a gum and is almost through, or when a small portion of a tooth has penetrated the gum, small areas of congested mucous membrane appear, and are of great aid in the diagnosis.

The symptom next in frequency is the hemorrhage into the skin. These may occur in any part of the body, in any number or distribution. The commonest lesions are scattered small bluish macules. These may involve larger areas, forming at times extensive ecchymoses, and occasionally the eyeball may be pushed forward by hemorrhage into the orbit.

The commonest symptom of internal hemorrhage is hematuria. This is seen in quite a large proportion of severe cases. Occasionally it is the earliest and most prominent symptom.

Anemia is slight in the early stages of the disease, but often becomes marked in advanced cases. The blood shows the ordinary characteristics of a secondary anemia.

FIG. 123



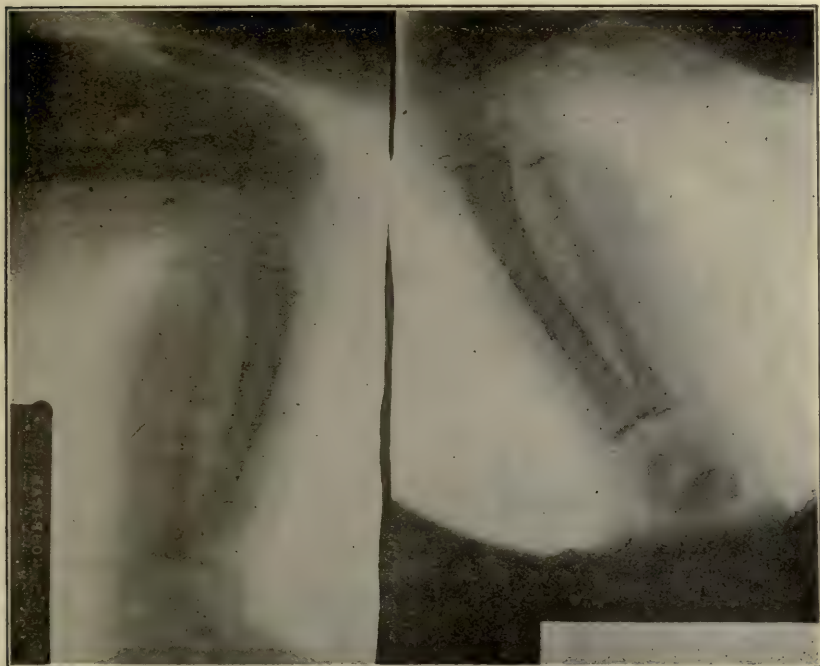
Infantile scorbutus. (Second month of disease.) Female, 10 months old

In addition to the symptoms of pain and tenderness, the infant keeps the affected limb perfectly still, so that, unless it were understood that it is pain which prevents it from moving the limb, it might be supposed that it was paralysis; in fact, this symptom in scorbutus has been termed pseudo-paralysis. It has nothing to do with true paralysis, and corresponds to what is seen in rheumatic affections of the joints.

DIAGNOSIS.—The diagnosis of infantile scorbutus is usually not difficult, if the characteristic symptoms of the disease be kept in mind. The chief cause of errors in diagnosis, is the fact that the frequency, or even the very existence, of infantile scurvy is often forgotten. The existence of tenderness over the bones, especially over more than one bone, in an infant between six and eighteen

months, is always suspicious of scurvy. If there is evidence of hemorrhage in any other part of the body, the probability of scurvy is greatly strengthened. The association of tenderness over the limbs with reddened, swollen gums is diagnostic. When the characteristic lesion of the gums is absent, the differential diagnosis of scurvy is mainly based on the absence of the characteristic signs of other conditions for which scurvy might be mistaken.

FIG. 124



Scorbutus. The plate shows the "white line"

The X-ray findings in scurvy are also characteristic. The earliest sign is the so-called "white line," an area of increased density at the junction of the epiphysis and the diaphysis. This is almost constant in scurvy, but is also seen in some other conditions. Usually the thickening of the periosteum, and its separation from the shaft by hemorrhage, can be made out in roentgenograms.

The diagnosis of infantile scorbutus is to be made from rheumatic fever, rachitis, purpura, syphilis, acute anterior poliomyelitis, tuberculous joint disease, osteo-myelitis, sarcoma, and acute nephritis.

RHEUMATIC FEVER.—Scurvy is most frequently confounded with rheumatic fever. In view of the extreme rarity of rheumatism in infants, especially under one year, pain, tenderness, and swelling

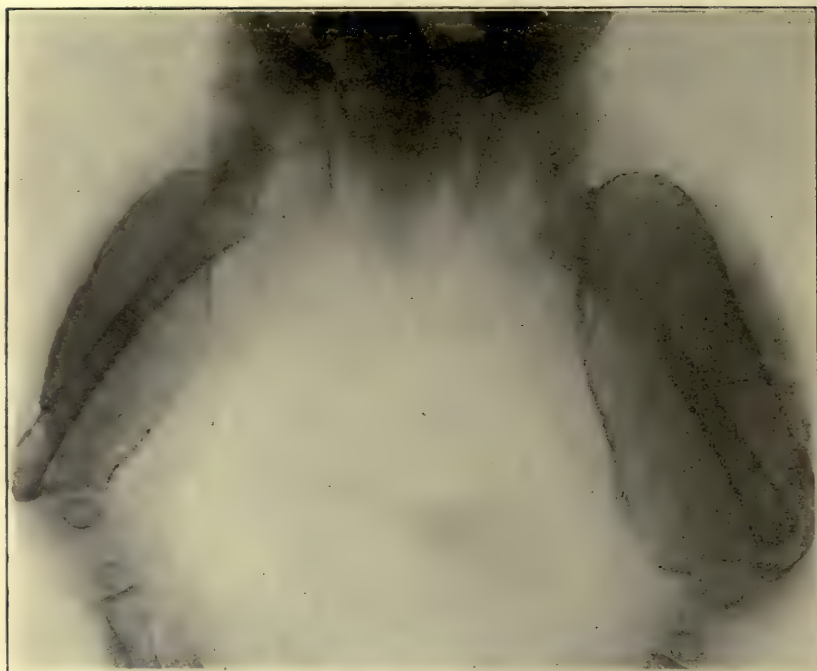


FIG. 125—Scorbutus. The plate shows enormous subperiosteal hemorrhages

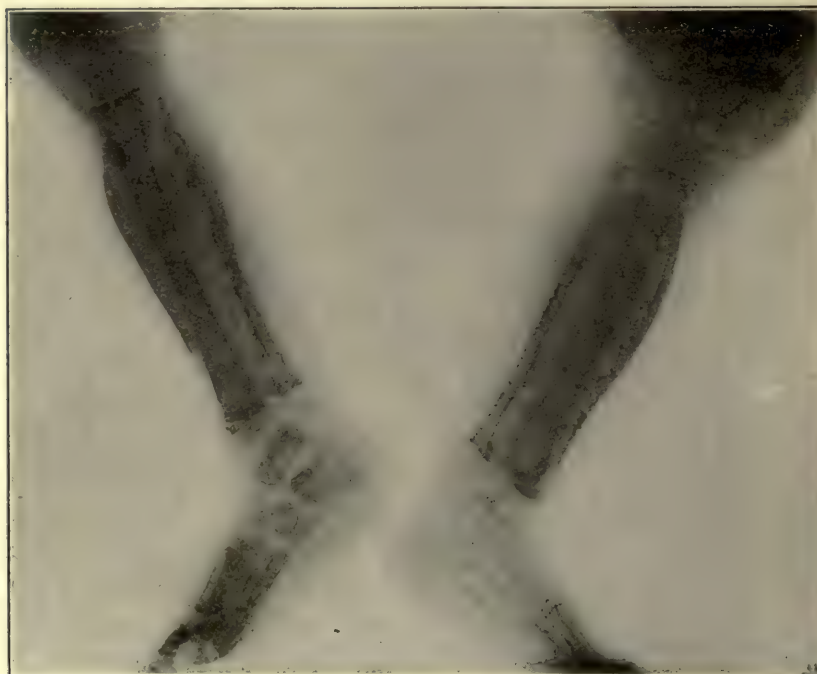


FIG. 126—Scorbutus. Showing large subperiosteal hemorrhages

of the limbs in an infant should always suggest scurvy. In scurvy, careful examination will usually show that the tenderness is connected with the bones rather than with the joints.

RACHITIS.—In cases of scorbutus not complicated by coexistent rickets, the diagnosis is based on the absence of the characteristic signs of rickets, such as the rosary, enlarged epiphyses, rachitic head, and so forth. In cases in which rickets is also present, the recognition of scurvy is sometimes more difficult. If the characteristic lesion of the gums is present, or if there are ecchymoses on the skin, or hematuria, the existence of scurvy can be recognized at once.

FIG. 127



Scorbutus. Showing small subperiosteal hemorrhages

If these confirmatory signs are absent, the physician should remember that tenderness is a rare symptom in rickets, but always constant in scurvy. The swelling near the epiphysis in scurvy can usually be distinguished from the enlargement of the epiphysis in rickets. Doubtful cases should be treated for scurvy, and the rapid response to treatment will confirm the diagnosis. The question can almost always be positively settled by X-ray examination.

PURPURA.—This disease is characterized by hemorrhage, particularly into the skin. It is very rare in infants. It can usually be excluded by the tenderness of the shafts of the long bones in scurvy.

SYPHILIS.—Occasionally cases of syphilis are seen in infancy, characterized by painful swellings about the ends of the long bones, due to syphilitic osteo-chondritis. This condition can usually be excluded, either by the absence of other signs characteristic of syphilis and described under that disease, or by the presence of the characteristic lesions of the gums or of hemorrhages in some other part of the body. Examination by roentgenogram will also make clear the distinction between the two conditions. It should also be remembered that syphilitic osteo-chondritis usually occurs before the fifth month.

POLIOMYELITIS.—The unwillingness of infants to move the limbs has led to scurvy being mistaken for poliomyelitis. Careful examination will show that in scurvy the condition is only a pseudo-paralysis. Poliomyelitis is a febrile disease of acute onset, but this stage is often overlooked. There may be pain on motion in poliomyelitis, but there is usually no tenderness to pressure as in scurvy. When any other signs of scurvy are present, there should be no difficulty in recognizing the condition.

TUBERCULOUS JOINT DISEASE.—This condition shows pain on motion, with muscular spasm, but usually no tenderness to pressure over the bone. Swelling, when present, is in the joints in tuberculosis, not over the bone, as in scurvy. The presence of hemorrhage elsewhere is diagnostic of scurvy. Roentgenograms will settle the diagnosis in doubtful cases.

OSTEO-SARCOMA.—I have seen cases of scurvy in which the swelling was mainly confined to one limb and very large, mistaken for osteo-sarcoma. The other signs of scurvy were present, but overlooked. The extreme tenderness of the swelling is the characteristic feature of scurvy.

OSTEOMYELITIS.—Scurvy is frequently mistaken for osteomyelitis by those who forget the possibility of the former. Osteomyelitis is usually confined to one limb, is characterized by a continued high febrile reaction, and by leucocytosis, and lacks the tendency to hemorrhages in other parts of the body. The diagnosis can be settled by X-ray examination.

ACUTE NEPHRITIS.—Albumin is often found in the urine in scurvy, and I have seen cases in which hematuria was the only symptom, mistaken for acute nephritis. The absence of edema, the absence of a diminished quantity of urine, and the absence of many casts, all point to scurvy. The rapid disappearance of the hematuria under antiscorbutic treatment, will finally confirm the diagnosis.

PROGNOSIS.—Scorbutus is very variable in its duration. If left untreated, all the symptoms may become more pronounced and the infant may finally die of exhaustion. When properly treated,

and uncomplicated by any other disease, the prognosis is very favorable. There is no disease in which the favorable reaction to treatment is more rapid. Tenderness disappears almost at once, and the hemorrhages into the gums, skin, and urine, clear up very rapidly. The swelling over the bones caused by subperiosteal hemorrhage persists somewhat longer, but recovery is always finally complete. The only danger in scorbutus comes from the disease remaining so long unrecognized, that the vitality of the infant has been greatly lowered. In such cases, death may occur from gastro-intestinal disease or intercurrent infection.

TREATMENT.—The treatment of infantile scorbutus is very simple and consists in two things, plenty of *raw milk*, and *orange juice*.

Fresh cow's milk should be used, modified to suit the peculiarities of the infant's digestive powers and requirements. It is advisable that the infant should take as much milk as he can digest, and therefore the modification should be made as strong as is possible without producing signs of indigestion. Slightly undigested or green movements should not be a contraindication to giving a strong food, provided that these symptoms are not increasing. A good milk supply is essential, in order to avoid the necessity of pasteurization, which is contraindicated in scurvy, unless a good milk supply cannot be obtained. In such a case, a wet-nurse should be engaged if possible.

With a diet of raw milk, or human milk, complete recovery will occur without further treatment. The process of recovery will, however, take considerable time, and can be much hastened by the addition of fresh fruit juice to the diet. The juice of any ripe fruit is effective, but *orange juice* is to be preferred, as it can be easily obtained, and babies usually like it. It rarely disturbs digestion, and is less likely to do so when given in a single daily dose than when given in divided doses before each feeding, as is usually recommended. The daily dose should be one ounce, given an hour before the morning feeding. It may be diluted or sweetened, if taken better in this way. Orange juice is all that is necessary to effect a complete and rapid cure of scurvy. No drug has any influence upon the disease.

In older children, whose diet contains other things than milk, potato is a valuable antiscorbutic, if it can be digested. All fresh vegetables which can be given, are also antiscorbutic. These things should only be given, however, when the patient has reached the age which permits their introduction into the diet.

In the prophylaxis of scorbutus, the principal thing is the avoidance of the patent foods, and all foods prepared by heat. If babies are breast-fed, they will almost never develop scorbutus. The ques-

tion of the pasteurization of the cow's milk used in the artificial feeding of infants, is often raised in connection with the prophylaxis of scorbutus. Is it undesirable to pasteurize milk on account of the danger of the development of scurvy? It has been shown that scurvy is more likely to develop from the boiling or prolonged heating of milk, than from simple pasteurization. Still, it is probable that even pasteurization partially at least, destroys the antiscorbutic substances in milk, as scurvy develops more often in infants fed on pasteurized milk than in those fed on raw milk. The question therefore depends on the danger to be apprehended, from scorbutus with pasteurized milk, and from bacterial infection with raw milk. This has been discussed in the division on Feeding. In general, it depends on the character of the milk supply. With certified milk, or milk produced under properly inspected conditions, raw milk is preferable. With any other milk supply, the dangers from infection are greater than the dangers from scorbutus, and the milk should be pasteurized.

PROBLEMS AND RESEARCH.—Investigations on the subject of scurvy have been made by animal experiments, by metabolism experiments on infants, and by blood coagulation experiments.

Holst and Fröhlich first produced experimental scorbutus in animals in 1907. They, with Furst, have since continued the work, and have published numerous papers. Their work conclusively proved that scurvy is not due to starvation or inanition, but to the lack of some essential food element. Scurvy has been produced by various diets, and cured by various articles of diet. The antiscorbutic properties of various vegetables have been investigated, and it has been found that while they are weakened, they are not entirely destroyed, by cooking. Variations in the antiscorbutic power of various vegetables and fruit juices to withstand heat and drying have been demonstrated. Other observers have confirmed and extended these results. None of these experiments has thrown any light on the nature of the antiscorbutic bodies, although efforts have been made to isolate them by extraction, dialysis, and other methods.

A few studies have been made on the metabolism of scurvy. While the results are interesting, they have as yet thrown no light on the essential nature of the disturbance seen in the disease.

Hess and Fish have recently published an interesting study bearing on the question of the cause of the hemorrhages in scurvy. They studied the coagulation factors in infantile scurvy, and were unable to demonstrate any marked decrease in the coagulation time of the blood. There was no evidence of calcium deficiency or of antithrombin excess, and the platelet count was normal. They then studied

the blood vessels by means of what they term the "capillary resistance test," which consists of binding a limb in such a way as to increase the blood pressure in the vessels, and observing the occurrence of hemorrhage. They found that there was a weakness of the vessel walls in scurvy; this is, however, not pathognomonic of scurvy, but is found in other hemorrhagic diseases. This work supports the theory that the hemorrhages of scurvy are not due to changes in the blood secondary to disease of the bone marrow, but are due to a condition of the blood vessels which is a primary manifestation of the disease.

THE VITAMINS.—The subject of scorbutus cannot be concluded without reference to the interesting and suggestive theories of Funk, published in 1914. He believes that there exists in food certain substances which play an important rôle in physiology and pathology, and which he calls vitamins. He believes that these substances are essential to proper metabolism and nutrition, and that their absence causes certain diseases, such as scorbutus, beriberi, pellagra, and rickets. He calls these diseases the "avitaminoses." He shows from his own work and that of others that milk contains substances which favor the growth of young animals, and attributes the development of scurvy in infants to the taking of food not containing milk, or containing an insufficiency of milk, or consisting of heated milk. He believes that the vitamins are the substances which are sensitive to heat; also that at times, raw milk or even breast-milk contains an insufficiency of vitamins. He advances evidence to show that the amount of vitamins in cow's milk varies with the food of the cows; cow's milk contains less of the vitamins in winter when the cows are eating dry fodder than in the summer when their fodder is green. He also calls attention to a diminution of the vitamins in the milk of women who are underfed.

The premises of Funk's conclusions are not yet established facts. Nevertheless the theory fully covers and explains all the clinical and experimental facts which have been established as to scurvy. It is possible that the subject of the vitamins, and the etiological relationship of scurvy to such diseases as beriberi and pellagra, will be the subject of much study in the next few years.

PURPURA

The term purpura is retained here chiefly on account of its frequent appearance in pediatric literature. Purpura is not a disease, but a symptom-complex, characterized by a tendency to spontaneous hemorrhage. Many writers, especially in Europe, recognizing the great variety of conditions in which hemorrhages occur, call this syndrome characterized by a tendency to hemorrhage the "hemor-

rhagic diathesis." This term is objectionable for several reasons. In the first place the word "diathesis" implies that there is some constitutional factor underlying this tendency toward spontaneous bleeding; this has not been proven, and is supported by little evidence. In the second place it groups together cases in which the hemorrhage is the primary essential feature of the disease, and cases in which the hemorrhage is secondary to proven causes. Among the conditions characterized by hemorrhage, three represent fairly definite disease entities, namely, hemorrhagic disease of the newborn, scorbutus, and hemophilia. These diseases are consequently considered separately. There remains only a symptom-complex, and it is to this symptom-complex that the term purpura is here applied.

Spontaneous hemorrhages are often seen in pathological conditions of which the nature is definitely known. In such cases, the hemorrhage is obviously a symptom of the known disease, and the hemorrhagic symptom-complex may be classified as *symptomatic purpura*. In a number of other cases, the spontaneous hemorrhages are apparently the primary pathological condition. It is probable that in these cases also the hemorrhagic symptom-complex is symptomatic of some other primary pathological condition, but as the underlying cause is unknown, this group may be conveniently described as *primary purpura*, the term primary being equivalent to "of unknown cause." In view of the fact that in many cases belonging to this group, abnormal changes in the composition of the blood have been demonstrated, it might seem that the primary purpuras should be classified with the diseases of the blood. The changes in the blood, however, do not appear to affect the cellular elements of the blood in such a way as to form a definite lesion, as is the case in such diseases as leukemia and pernicious anemia. Moreover the blood changes are strongly suggestive of either nutritional disturbance, or of the action of toxin. It is for this reason that the primary purpuras are classified among the disturbances of nutrition and metabolism.

SYMPTOMATIC PURPURA

ETIOLOGY.—The various known diseased conditions in which symptomatic purpura is seen at times, suggest the following factors in etiology:—Infection, toxemia, nutritional disturbance, and disease of the blood. Mechanical hemorrhages, such as are seen in pertussis and epilepsy, are also sometimes classed as purpura. At times after protracted illness, when patients first stand or walk, hemorrhagic spots appear on the lower extremities. It is probable that in such cases the cause is partly nutritional and partly mechanical.

INFECTION.—Purpura is often seen as a symptom of various known acute infections. It is most constant as a symptom in malignant endocarditis, but is sometimes seen in measles, scarlet fever, small-

pox, vaccinia, typhus fever, epidemic meningitis, diphtheria, septicemia, and pyemia. The frequency of its presence in infectious disease of the newborn has already been described. In these acute infections, the hemorrhagic symptom-complex is probably due to an altered condition of the blood, which in turn is caused by the bacterial toxins of the primary disease.

TOXEMIA.—Certain drugs, and certain known chemical poisons, can produce spontaneous hemorrhages. The effect on the blood of benzol poisoning is well known. Such drugs as potassium chlorate, quinine, and phosphorus have produced cutaneous hemorrhage when given in excessive dosage, or in long-continued administration. The pronounced tendency to hemorrhage seen in cases of jaundice is certainly of toxic origin. This group is distinguished from the first only in that the toxins are not of bacterial origin.

NUTRITIONAL DISTURBANCE.—Purpura often occurs as a late symptom of various known diseases in which marked disturbance of nutrition is a prominent feature. While most of these diseases are of infectious origin, the occurrence of hemorrhages late in the course of the disease, points toward a nutritional injury rather than a toxic injury. Also, purpura is seen in cachectic conditions which are not of infectious origin, such as starvation, functional gastrointestinal disease, and malignant disease. Cachectic purpura is seen particularly often in the wasting diseases of infancy, and is met with in tuberculosis, meningitis, bronchopneumonia, and empyema. There is little doubt that the symptom is due to a disturbance of nutrition, either of the blood, or of the blood vessels. An example of a hemorrhage of nutritional origin is seen in scurvy.

DISEASES OF THE BLOOD.—Purpura is a fairly common symptom in primary diseases of the blood and blood-making apparatus, such as pernicious anemia, leukemia, and pseudo-leukemia.

SYMPTOMS.—The hemorrhages in symptomatic purpura are usually limited to the skin, and appear as hemorrhagic spots of various sizes and varying distribution. Rarely hemorrhage from the mucous membrane is seen.

DIAGNOSIS.—The hemorrhagic character of the spots is recognized by the fact that the color cannot be caused to fade by pressure. The diagnosis of the symptomatic character of the purpura depends upon the finding of an adequate cause.

PROGNOSIS.—The prognosis is that of the disease to which the purpura is secondary. In most of these conditions the appearance of purpura is a bad prognostic sign.

TREATMENT.—The treatment of symptomatic purpura is that of the cause.

PRIMARY PURPURA

ETIOLOGY.—The purpura is called primary when there is no recognizable cause. There has been much research devoted recently to the hemorrhagic diseases of early life, as a result of which a certain amount of knowledge has been gained, which can form a basis for a theoretical conception of the nature of the purpura, and of the factors probably concerned in its etiology.

The symptom-complex called purpura is characterized by hemorrhage, and the tendency to spontaneous bleeding must be due to one or both of two immediate causes. The first is an abnormal composition of the blood, which lessens its coagulability. The second is an abnormal condition of the blood vessels which increases their permeability.

The coagulation of the blood has been extensively studied in recent years. While the full mechanism is still not perfectly understood, considerable advances have been made. In most of the cases of primary purpura which have been studied, a defective power of coagulation has been found in the blood. This is shown partly by a delay in the coagulation time, and partly by the formation of a clot of diminished firmness and contractility. Most of the cases studied have been typical cases of the clinical type called "purpura hemorrhagica," and the most usual finding suggests that the diminished coagulability is due to a deficiency in the prothrombin, the substance derived from the blood platelets. A marked diminution in the blood platelet count has been found repeatedly in purpura hemorrhagica. While this may not apply to all cases, and while some cases of purpura may show some other abnormality in the blood, this finding suggests at least that *there is often if not always in purpura an abnormal condition of the blood itself*, which manifests itself in defective coagulation.

The second possible factor, an abnormal condition of the walls of the blood vessels, has not yet been extensively studied. It cannot, however, be excluded in a condition which is not a single disease entity, but a symptom-complex due possibly to a variety of causes.

If the spontaneous hemorrhages of purpura are due to an abnormal condition of the blood or blood vessels, what causes this abnormal condition? It is not, as in hemophilia, an inherited constitutional anomaly, for the occurrence of purpura suddenly, at any age, without obvious cause, suggests that the cause is not an inherent tissue defect, but that it is acquired. In reaching an idea as to the probable cause of primary purpura, the varied etiology of the secondary, symptomatic purpuras is most suggestive. These secondary purpuras are associated with a number of known conditions, and *infection*, *toxemia*, and *nutritional disturbances* are the most probable causes of the hemorrhage. We know that all of these factors can exist with-

out definite recognition. It is probable that there are numerous types of bacterial infection which have not been recognized, and many writers believe that the chief cause of primary purpura is such unrecognized infection. Furthermore, we know comparatively little about the function of nutrition and metabolism, particularly about the so-called intermediary metabolism. There is much evidence that suggests that toxic products may be formed through a disturbance of metabolism of unknown nature. Again, emaciation is not a necessary manifestation of all nutritional disturbances, as is evident by such conditions as rickets and scurvy, in which loss of weight is not an essential feature. We must therefore admit that it is very probable that there are disturbances of metabolism of which we know nothing, but which may easily lead to the formation of toxic products, and to disturbed nutrition.

The blood is the result of the very complex work of all the organs and tissues of the body. Its composition probably depends on the activity of many organs, and of many cells, acting both as individual entities and in relation with each other. It is therefore easy to conceive how infection, disturbance of metabolism, toxin formation, and impaired nutrition, could impair the composition of the blood itself, and cause a defective condition of the walls of the blood vessels. I believe that these are the probable causes concerned in the production of purpura, and that unrecognized infection is probably the most frequent factor. The symptoms of the various clinical types of purpura are strongly suggestive of infection and toxemia, and also of a varied etiology. We shall be obliged to speak of primary purpura until the nature of the disturbances, which are the real primary conditions of which spontaneous hemorrhage is the symptom, is more fully understood.

Primary purpura is more common in children than in adults. It is met with at all ages, although more often in older children than in infants. It is commonest between the ages of two and ten years. The sexes are about equally affected. There is no constant association with any particular predisposing cause.

PATHOLOGICAL ANATOMY.—The pathological anatomy requires no detailed description, the essential lesion being the hemorrhage. The variation in the extent and location of the hemorrhages is so great, that enumeration is cumbersome and unnecessary. The changes in the blood are confined to its finer composition, and nothing abnormal is noted on ordinary examination, other than the characteristics of a secondary anemia, the severity of which is in proportion to the amount of the hemorrhage.

SYMPTOMS.—Purpura has been divided upon a purely clinical basis into various types. This division bears no definite relation to

the probable etiology of the disease, although it is possible that some such relation may be found in the future, when the various etiological factors are more fully understood. The division into clinical types is retained for purposes of clinical description only, the various types not representing definite disease entities.

PURPURA SIMPLEX.—This is the commonest form of primary purpura in children, and in it the hemorrhage is confined to the skin. There may be moderate constitutional disturbance, which may accompany the hemorrhages, or may precede them for one or two days. The general symptoms are malaise, loss of appetite, and slight fever; there may be a disturbance of digestion with vomiting or diarrhea. The hemorrhages appear suddenly, and consist of small petechiae. The spots are small, varying in size from a pin-head to a pea, and are of a bright red color. As the spots fade, they become brownish-purple, and disappear in a few days. The distribution of the spots is very variable; certain parts of the body only may be involved, or the whole body may be covered. The petechiae usually appear first on the lower extremities. The spots in the involved areas are usually thickly scattered, but there may be only a few spots widely scattered on various parts of the body. The spots are likely to appear in successive crops, coming sometimes in new areas, and sometimes in areas where a former crop is fading or has faded. Often when the child gets out of bed, a fresh crop will appear on the legs.

The course of the disease is usually from one to three weeks, but relapses are common, and attacks may continue to come at short intervals for a considerable period. I have seen cases in which the child was unable to get out of bed for several months without the appearance of fresh spots. The prognosis is good, although it is best not to give an unqualifiedly favorable prognosis, because occasionally a mild simple purpura has suddenly developed into one of the severe and fatal types.

PURPURA RHEUMATICA (Peliosis Rheumatica; Schönlein's Disease). This type resembles simple purpura in every way, except that there is an additional symptom, namely, arthritis. The joints are painful on motion, and show some swelling. This type may be considered a primary purpura with an associated arthritis, or a symptomatic purpura secondary to an infectious arthritis. The association with rheumatic fever is, however, not very definite. The arthritic symptoms are less severe, and the heart is not involved. There is a more frequent association with certain other cutaneous lesions, particularly erythema exudativum, urticaria, erythema nodosum, and angio-neurotic edema. This type is strongly suggestive of a toxic origin, but whether the toxin is derived from bacteria or from a disturbance of metabolism is unknown.

The course of rheumatic purpura is from one to three weeks. Relapses may occur. The outcome is usually favorable.

PURPURA ABDOMINALIS. (Henoch's Purpura.)—This type closely resembles rheumatic purpura, except that it is more severe, and gastro-intestinal symptoms are prominent. The symptoms are more or less malaise, and pains not especially localized, but chiefly occurring in the extremities and back, sometimes accompanied by slight edema of the part affected. These early symptoms of pain occur in one or more joints, usually on the outer sides, and sometimes there are swelling and redness simulating rheumatic fever. In this stage there may be a sudden rise of temperature. Accompanying these symptoms there may be a few purpuric spots, but, as a rule, there is a period of several days between the appearance of the pains in the joints and the purpuric appearance on the skin. The purpuric spots may coalesce, and thus form ecchymoses of various sizes and colors. They are very apt to begin on the lower leg and spread up to the thighs, genitals and body. Somewhat later, intestinal symptoms develop. While the purpura is spreading there is severe colic, and the pain is very intractable to treatment. The abdomen is retracted and tender. There is obstinate vomiting. The pulse is weak, and the face has an anxious expression. There is more or less diarrhea, which usually occurs at the end of an attack of colic. The colic and vomiting sometimes last for one or two days. There may be a little blood in the vomitus and in the movements. The vomiting then diminishes, the colic ceases, and later the diarrhea stops, the pain in the joints passes away, the purpuric spots gradually fade and disappear, and the child, although left in an exhausted condition, is otherwise well.

There are very apt to be relapses, which may appear within a few days or not for several days.

These are the symptoms of a typical case; but there are many variations. As a rule, the younger the child the more typical is the case. Sometimes the purpuric spots closely simulate urticaria. They may occur, although rarely, in the mouth. They sometimes simulate the lesions of erythema nodosum. The attacks of colic have a paroxysmal character. There may be swelling of the joints.

This disease is rarely fatal unless it is complicated by some such disease as nephritis or endocarditis.

PURPURA HEMORRHAGICA. (Morbus Maculosus Werlhofii.)—This is a very severe form of primary purpura, characterized by hemorrhages from the mucous membranes as well as cutaneous hemorrhages. Bleeding from the mucous membranes is present from the start, and may even precede the cutaneous ecchymoses. There may be bleeding from the nose, mouth, pharynx, stomach, or intestines.

The most frequent symptoms are the vomiting of blood, and the passage of bloody discharges from the bowels. The urine may contain enough blood to be bright red in color. There may more rarely be bleeding from the ear, conjunctiva, or female genitals. Ecchymoses may sometimes be seen on the visible mucous membranes, and hemorrhages may occur into the retina or choroid of the eye.

Purpuric spots on the skin are always present. They are most often large ecchymoses, which appear suddenly in various parts of the body.

Constitutional symptoms, such as fever, and malaise, are often present, but not constant. All the abdominal symptoms described under Henoch's purpura may be present. Anemia and prostration finally become marked, and the loss of blood may be sufficient to cause death.

The course of the disease is very variable, the symptoms usually lasting from one to six weeks. Death may occur from loss of blood, or the patient may pass into a condition suggesting general sepsis, with high fever, delirium, great prostration, and irregular failing pulse, which finally ends fatally. A certain number of cases recover, but the prognosis in general is unfavorable in early life, depending on the age of the patient and the extent of the hemorrhage.

PURPURA FULMINANS.—A very malignant purpura hemorrhagica may occur, sometimes proving fatal within twenty-four hours. This form of purpura is usually spoken of as purpura fulminans. It is most commonly met with in infants and in very young children, and is characterized by excessive cutaneous hemorrhages which develop with great rapidity, death sometimes taking place before there has been any hemorrhage from the mucous membranes. There is high fever, vomiting, marked prostration, cerebral symptoms, and the disease has all the characteristics of an acute general infection.

DIAGNOSIS.—The diagnosis of purpura depends first upon the recognition of the hemorrhagic spots on the skin. The eruption is recognized as hemorrhagic by the failure of the spots to disappear on pressure. The diagnosis of the "primary" nature of the purpura can only be made by a careful exclusion of all the conditions in which purpuric spots sometimes appear as a symptom. The diagnosis of the clinical type of purpura depends on the associated symptom-complex.

TREATMENT.—The etiology of purpura being unknown, and probably multifactorial, there is no specific treatment for primary purpura. No drug has any influence on the underlying causes of the disease. The treatment must therefore be symptomatic.

The only serious symptom requiring treatment is the hemorrhage.

The clinical types of purpura characterized only by cutaneous hemorrhages, are not especially dangerous, and the hemorrhage requires no treatment. Simple purpura, purpura rheumatica, and Henoch's purpura, without hemorrhage from the mucous membranes, all run a definite course, and tend toward recovery. Not enough is known about the etiology to afford a definite basis for prophylactic treatment directed at preventing relapses, but in cases with a marked tendency toward relapse, serum therapy may be tried. Horse serum, rabbit serum, and human serum all have a theoretical basis in the hemorrhagic diseases. Their relative value is not definitely determined, but the evidence points toward human serum as the most valuable, and horse serum as the least; just the reverse of the ease with which the various sera can be obtained.

In simple purpura, no other symptoms need be treated. Rheumatic purpura may be symptomatically treated like rheumatic fever, with salicylates. Henoch's purpura should be treated like an acute infection with gastro-intestinal symptoms.

Purpura hemorrhagica, or any form of purpura in which blood is lost from the mucous membranes, is a dangerous condition, and requires active treatment of the hemorrhage. Various methods of treatment have been recommended from time to time for the hemorrhagic diseases, each based on some particular theory of the pathology of the condition. The evidence at present is against the value in purpura of injections of gelatin, of injections of adrenalin, and of the administration of calcium salts. There remains, serum therapy. Horse serum, rabbit serum, and human serum or human blood, all have theoretical evidence in their support, because any of them may supply the element which causes diminished coagulability of the blood. There is clinical evidence in favor of all three sera. Human serum is usually free from the possible danger of anaphylaxis, and experiment suggests that it is more potent than rabbit serum, while rabbit serum is more potent than horse serum.

In comparatively mild cases, horse serum may be tried first, given in doses of 30 c. c. or more, according to the severity of the hemorrhage. Rabbit serum may be tried first, or after the failure of horse serum.

In all severe cases, human serum should be preferred. The donor having been obtained, about 60 c. c. of blood should be withdrawn with a sterile syringe from the vein at the bend of the elbow. Of this, 30 c. c. should be injected subcutaneously at once, and the rest should be set aside to furnish serum for further treatment. In the subsequent injections, this serum may be used, and if possible, from 10 to 30 c. c. should be given every four to eight hours, according to the course of the case.

In any case in which the patient is so severely ill from loss of blood

that life is threatened, or if the injections of whole human blood or human serum are not followed by definitely recognizable improvement, the safest treatment is by transfusion. Whenever a surgeon can be obtained who is familiar with the rather formidable technique of this operation, it is the most promising method of treatment.

Serum therapy, and transfusion are the only available methods of checking the bleeding in purpura hemorrhagica, and are often strikingly successful. They do not always succeed, however. I have recently seen a case which died of hemorrhage in spite of repeated transfusions. This only emphasizes the probable multiplicity of the factors which are concerned in the pathology of purpura.

After convalescence from an attack of purpura, the anemia is to be treated with iron in the ordinary manner.

PROBLEMS AND RESEARCH.—The principal problem awaiting further research in connection with purpura, is that of etiology. The most promising field for investigation lies in the pathology of the blood. It is probable that the symptom-complex known as purpura, represents not only a variety of underlying causes, but also a variety of abnormalities in the blood and blood-vessels. The first step will be the recognition of all the various abnormalities in the blood and bloodvessels which are seen in purpura, and their classification. This problem has already been attacked. For a description of the known facts concerning the coagulation of the blood, the reader is referred to the Problems and Research in connection with hemorrhagic disease of the newborn in Division III.

It is probable that there are various types of purpura representing deficiencies in different elements of the group of factors concerned in blood coagulation. Deficient coagulability of the blood may be due to a deficiency of prothrombin (blood platelets), of calcium salts, of kinase, or of fibrinogen. It may be due to an excess of antithrombin. Finally, in some cases, the tendency to hemorrhage may be due to an abnormality of the vessel walls.

The problem of purpura has already been attacked along these lines. The principal abnormality of the blood found in purpura hemorrhagica appears to be a deficiency of prothrombin. Duke found in typical cases an enormous reduction of the blood platelets. This has been confirmed by other observers. A low platelet count has also been found in certain cases of symptomatic purpura. Furthermore, purpura has been produced experimentally in animals by injections of the serum of an animal immunized with blood platelets. It has also been produced in rabbits by injections of diphtheria toxin, which reduced the platelet count. All this work, however, by no means proves that this is the only blood deficiency present in purpura.

Some evidence has been brought forward that purpura is not due

to a deficiency of calcium. It will, however, be necessary to investigate many cases of purpura by many different methods before a final solution of the problem is reached. The methods of investigation now in use are the following: Measurements of the coagulation time; studies on the firmness of the clot; studies on the effect of adding calcium salts; studies on the effect of adding defibrinated human blood; studying the effect of the purpuric blood on normal blood; artificial extraction of the thrombin in pure form; measurement studies on the condition of the vessels by capillary resistance tests. It is possible also that increasing knowledge of the obscure manifestations of disturbed metabolism may throw some light on the etiology of purpura.

HEMOPHILIA

Hemophilia is characterized by excessive and prolonged bleeding following an injury, and is a clear-cut clinical entity. It is an inherited, constitutional anomaly.

ETIOLOGY.—The inherited tendency of the disease is one of the factors which sharply differentiates hemophilia from other hemorrhagic conditions. The disease nearly always affects males, and is usually transmitted through healthy females. The tendency to hemorrhage usually persists unchanged throughout the life of the patient. There is no evidence of any connection with purpura, scurvy, infection, toxemia, or any other diseased condition.

The immediate cause of the hemorrhage is usually a mechanical injury to the tissues. From a wound which would ordinarily produce slight bleeding, the hemorrhage is excessive and prolonged. At times hemorrhage is produced by an injury so slight that bleeding would not follow in normal persons. Occasionally the hemorrhage appears to be spontaneous, but this is probably due to the fact that in hemophilia, slight mechanical shocks such as are incidental to ordinary daily life, may cause bleeding.

The nature of the constitutional abnormality in hemophilia is still an open question. Many theories have been advanced to explain the hemorrhages, such as an abnormal thinness of the walls of the bloodvessels, high blood pressure, disproportion between the total amount of blood and the capacity of the vascular system, and various abnormalities in the composition of the blood. There is no evidence in favor of any of these theories except the last, and the weight of modern opinion inclines toward the opinion that the inherited anomaly in hemophilia involves the blood.

As to the nature of the blood deficiency, various investigators claim various abnormal conditions, such as a diminution in the amount of fibrinogen, calcium salts, prothrombin, or thrombokinase, or an excessive amount of antithrombin. Lack of calcium has been

shown not to be the cause, and there is no convincing evidence of a deficiency of blood platelets, or of thrombokinase. The present state of the matter lies between a deficiency of fibrinogen, and an excess of antithrombin.

Cases are occasionally met with having all the clinical features of true hemophilia, but with no evidence of heredity. These cases occur later in life, affect both sexes, and probably represent an accidental sporadic type of unknown cause. Etiologically they probably belong with the purpuras.

SYMPTOMS—In hemophilia the first manifestation of the disease does not often appear until the second year, or even later. This is probably due to the fact that wounds and traumatic injuries are uncommon until the child begins to run about. Occasionally there is excessive bleeding from the umbilicus at birth, but this is rare in hemophilia. The first hemorrhage may be either traumatic, or apparently spontaneous. In traumatic hemorrhage, a very slight wound, or the drawing of a tooth, is followed by severe and prolonged bleeding. A slight contusion may cause an extensive hematoma between the muscles. The commonest site of spontaneous hemorrhage is the nose, but bleeding is occasionally seen from the mouth, intestines, stomach, urethra, and lungs.

Hemorrhage into the joints is a fairly common form of apparently spontaneous hemorrhage in typical cases. The joints normally are constantly subjected to mechanical shocks, and in hemophilia the ordinary activities of life are sufficient to produce hemorrhage. The blood in articular hemorrhage is not all absorbed, but becomes partly organized, and this leads to symptoms resembling arthritis. The articular symptoms of hemophilia have been described as a coördinate manifestation, but they are really the result of a former hemorrhage which has been overlooked. Repeated hemorrhage may finally lead to marked articular deformity.

The essential feature of the hemorrhages of hemophilia is their prolonged and uncontrollable character. Sometimes over a wound a crust may form and bleeding may cease externally, but continue into the subcutaneous tissue. Later, the accumulated blood breaks through, and then the hemorrhage is still more difficult to control.

There is a sporadic, accidental type, in which the hemorrhage resembles the bleeding of true hemophilia. This type is not inherited, usually appears later in life than childhood, and affects the sexes equally.

DIAGNOSIS.—The first hemorrhage of hemophilia so rarely occurs in the first week of life, that there is little difficulty in distinguishing from it the hemorrhagic diseases of the newborn. The only condition for which hemophilia might be mistaken is purpura hemor-

rhagica. In the latter the hemorrhage is always spontaneous, and there is almost always hemorrhage into the skin. The essential feature of hemophilia is that wounds and injuries tend to produce excessive hemorrhage. Even when the hemorrhage is apparently spontaneous, there is usually a history of previous excessive bleeding from a wound. The hereditary nature of hemophilia, and the absence of cutaneous petechiae, are further distinguishing points.

PROGNOSIS.—The first attack is rarely fatal. Many attacks may occur, without a fatal result, and the children may grow up and live indefinitely. Sometimes the tendency toward hemorrhage is outgrown in later life, but in typical cases it persists.

On the other hand, any attack, even from a slight cause, may lead to marked exsanguination, or even to a fatal ending. The chances are a little more than even that a patient showing signs of hemophilia in childhood will not live to enter adult life.

TREATMENT.—The hemorrhage from wounds is treated by the usual surgical measures for the control of bleeding, particularly compression. The treatment of severe cases is with serum, as described for purpura hemorrhagica. Transfusion should always be prepared for in every case, and used whenever the bleeding appears to be becoming dangerous.

PROBLEMS AND RESEARCH.—Hemophilia has been, and is being, investigated by the same methods as are used in the other hemorrhagic diseases, consisting chiefly of laboratory study of the factors concerned in the coagulation of the blood. Among the recent investigations is one of Whipple, showing increased antithrombin in hemophilia. Several investigators have found a normal platelet count in hemophilia, in contrast to the diminished count in purpura hemorrhagica. Hess has recently devised a test for antithrombin, and has found that in animals it can be increased considerably without danger. His recent work showed, by a functional test, evidence of fibrinogen deficiency in hemophilia, but not in purpura. This did not seem to be the sole deficiency, as the addition of fibrinogen is often unable to bring the clotting of the blood to normal. Lack of calcium has been shown not to be the cause of the bleeding in hemophilia, but Hess found one sporadic case due to calcium deficiency, which he called hemophilia calcipriva. The evidence is rather against abnormality of the capillaries as a factor.

Schloessmann found that a tissue extract, made from hyperplastic thyroid material, was effective as a local application in hemophilia. Hess found a tissue extract, made of ground-up tissue, which he calls thromboplastin, similarly effective. Several European investigators have advocated the subcutaneous injection of propeptone (peptone de Witte), believing it to be more effective than serum therapy

ACIDOSIS

In the broadest sense, the term acidosis refers to a diminished alkalinity of the blood. The physicochemical reaction of the blood, which depends upon the balance between the hydroxyl and hydrogen ion concentration, is fairly constant, even in acidosis. In acidosis, it is the titrable alkalinity of the blood which is diminished. Acidosis may be relative or positive. Relative acidosis is due to a deficiency of the bases which cause the normal titrable alkalinity of the blood; an example of relative acidosis is seen in severe diarrhea, and in indigestion from excess of fat. Positive acidosis is due to the production of acids in abnormal quantity. It is only positive acidosis which is to be considered here.

The most satisfactory definition of acidosis under this limitation is that of Cautley, who called it "an abnormal metabolism of carbon leading to the appearance of organic acids in the blood and urine, and to the formation of ammonia to neutralize these acids."

The only definite clinical evidence of acidosis obtainable is the finding in the urine of the so-called "acetone bodies" consisting of acetone, diacetic acid, and beta-oxybutyric acid. These acetone bodies are found in the urine in a great number of known pathological conditions. The most perfect example of a positive acidosis is seen in diabetic coma. The acetone bodies, however, appear very frequently in the urine of children, in conditions of known etiology. They are found in starvation and cachexia, in several known forms of drug poisoning, and in the so-called delayed anesthetic poisoning. They are found in hepatic disease of known type, such as acute yellow atrophy. They have been found in eclampsia, and in nervous disturbances due to fright. They are often present in the acute infections accompanied by high fever, such as the exanthemata, diphtheria, pneumonia, influenza, appendicitis. They are rarely found in the gastro-intestinal disorders of infancy, but are very common in those of later childhood. Frew, however, in his investigations at the Great Ormond Street Hospital, found transient acetoneuria in most babies who were changed from the breast to the bottle. It persisted for about three days, and was ascribed by Frew to carbohydrate starvation due to a temporary failure of digestion. In most of these cases, the presence of the acetone bodies is not accompanied by toxic symptoms. From this point of view, acidosis as manifested by the appearance of the acetone bodies in the urine, must be regarded simply as a symptom of disturbed metabolism, with no more clinical significance than has albuminuria in similar conditions. There would consequently be no need to discuss acidosis under a separate disease heading.

There are, however, certain cases in which there is a fairly con-

stant and definite symptom-complex of disease, which cannot be readily attributed to known pathological conditions. The symptoms which have particularly attracted attention are attacks of severe vomiting without obvious or discoverable cause, but with a definite tendency toward recurrence. In other cases the prominent symptoms are vomiting accompanied by marked symptoms of nervous-system intoxication, again without obvious or discoverable cause, but without a definite tendency toward recurrence. To these symptom groups the names *Recurrent Vomiting*, *Periodic Vomiting*, *Cyclic Vomiting*, *Acid Intoxication*, and *Acidosis*, have been applied.

In 1901, Marfan noted the appearance of acetonuria in recurrent vomiting, and in 1903 Edsall called attention to the large quantity of the acetone bodies found in the urine in the same disease. This led to a general discussion of whether the formation of the acetone bodies is the cause of the symptoms, or whether it is only a coordinate manifestation of the disturbance of metabolism.

ETIOLOGY.—The relation of the acidosis to the symptoms in recurrent vomiting and the so-called acid intoxication is not definitely known. The cause of the disturbance of metabolism which produces the clinical symptoms and the acetonuria is not definitely known. The literature of the subject is filled with conflicting theories, but it is necessary for a student of the subject to have some knowledge of the views most widely held.

HISTORY OF THEORIES.—Langmead in 1906, doubted that the acetone bodies were the cause of the symptoms and ascribed the production of acid poisons to deficient oxidation of the fats in the liver, in consequence of an impairment of hepatic function caused by either alimentary toxins, or bacterial toxins from other parts of the body. Ewing also considered the condition due to a disturbance of fat metabolism, caused by deficient hepatic function, associated with the absorption of poisonous putrefactive products from the intestine. Rachford considers the condition an autointoxication, functional hepatic derangement causing an accumulation of purin bodies in the blood.

Another group of writers believe that it is the glycogenic function of the liver which is primarily disturbed. The analogy of the acidosis of diabetes is suggestive here, and it is known that carbohydrate starvation can produce acetonuria. Janeway and Mosenthal thought carbohydrate starvation important in acidosis, but more recent work appears to show that the symptoms are not due to a deficiency of carbohydrate in the diet. It is fairly well established that the normal metabolism both of fat and of protein is largely dependent upon proper carbohydrate metabolism, and is greatly disturbed by a deficiency of carbohydrate. Sedgwick called atten-

tion to increased creatin and creatinin excretion during attacks of recurrent vomiting; this is evidence of a disturbance of the intermediary protein metabolism. Mellanby also found creatinuria in recurrent vomiting. He considers acidosis secondary to derangement of the glycogenic function of the liver. The disturbance leads to imperfect katabolism of the fats, with the formation of diacetic and beta-oxybutyric acids as intermediary products, and to imperfect protein metabolism and creatin formation due to carbohydrate insufficiency. The disturbed glycogenic function is due to absorption of alimentary toxins. He does not believe that the acidosis is ever the cause of the symptoms, because the quantity of beta-oxybutyric acid (the only toxic member of the acetone group) is never large, the quantity of the acetone bodies being always small compared with that seen in diabetes. The acidosis is only a symptom of the disturbance of metabolism. Mellanby's view is strengthened by the recent work of Underhill and Steele, who found in the urine lactic acid as well as creatin and creatinin—a definite evidence of disturbed carbohydrate metabolism.

Another group of writers lay stress on the unstable character of the nervous system in children as a cause of disturbance of metabolism. Ely in 1903, asserted that cyclic vomiting is a neurosis, and many writers have held this opinion. The most careful work on recurrent vomiting has been done by Howland and Richards, who ascribe the attacks to shock or excitement depending on the unstable state of the nervous system. Such a cause, they believe, leads to disturbed metabolism with diminished oxidation, and the circulation in the blood of unoxidized toxic substances. More recently Zade has published a similar theory. He believes recurrent vomiting to be a result of a sudden psychogenic upset of carbohydrate metabolism, and believes that the psychogenic origin explains many of the peculiar features of the attack.

Few writers have observed any marked connection between the diet and the occurrence of symptoms of acidosis. Kerley, however, believes that "the chief error in most cases rests in a defective oxidation, or in the giving of food substances of high carbon content in excess beyond the powers of normal oxidation." He believes diet important in prophylaxis and treatment.

Finally, a large group of writers have called attention to the frequency of acidosis in children exhibiting catarrhal conditions of the naso-pharynx, especially with adenoids and enlarged tonsils. This suggests a possible bacterial origin of the disturbance of metabolism seen in acidosis.

THE MOST PROBABLE THEORY OF ETIOLOGY.—I believe that the symptoms in recurrent vomiting and "acid intoxication" are due

to toxic products of disturbed metabolism. The products which actually cause the symptoms are unknown, the accumulation of the acetone bodies being only a coördinate symptom of the disturbance of metabolism.

I believe that the essential disturbance involves the carbohydrate metabolism, and that the frequency and severity of the attacks in childhood are partly due to the fact that the reserve supply of glycogen in the liver is not so great proportionately in childhood as in adult life. A disturbance of the glycogen-storing or glycolytic function of the liver would cause an insufficient supply of sugar, and this would induce an immediate disturbance of fat and protein metabolism. The result of the latter disturbance is the formation of the acetone bodies, and of other more toxic products.

The cause of the disturbance of carbohydrate metabolism which precipitates an attack, must next be considered. The key to this question lies in the known pathological conditions which are at times accompanied by acidosis. We find prominent among these conditions, *bacterial toxemia*, *alimentary toxemia*, and *disturbance of the nervous system* (eclampsia, etc.). We know that similar conditions frequently exist unrecognized, and it is highly probable that they are the cause of attacks of recurrent vomiting and acid intoxication which are apparently primary. Many children carry a chronic focus of infection, such as adenoids, diseased tonsils, or a chronically inflamed appendix. In many children there is a constant absorption of putrefactive products from the intestine, without recognizable symptoms. All these toxins act primarily on the liver, and cause an impairment of the function of carbohydrate metabolism, which is probably compensated elsewhere until an acute disturbance occurs. Such an acute disturbance may be caused by the cumulative effect of toxins, or by a sudden increase in toxic absorption, such as could appear in a *fresh infection*, or in an increased activity of the already existing infection, or after a dietary indiscretion. Perhaps more important in the production of such an acute disturbance, especially in recurrent types, is *nervous disturbance* such as is seen in *excitement or fatigue*. From these causes, there results a failure of the liver properly to perform its functions, and the symptoms of acute derangement of metabolism follow.

OCCURRENCE.—Our knowledge of the occurrence of acidosis is based chiefly on a study of the clinical type characterized by recurrent attacks of vomiting. The disease may occur in infancy, and in children approaching puberty, but it is commonest in the period of middle childhood, the first attack appearing most frequently between the ages of two and four years. The condition is about equally common in girls and boys. The disease is distinctly commoner in

private practice than in hospital practice, and frequently occurs in children with the best surroundings. The family history frequently shows neurotic antecedents, as well as rheumatism and a tendency to sick headaches and bilious attacks. The children are often of the highly-strung, excitable type, and subject to sea-sickness or car-sickness. They are not notably subject to digestive disturbance, but often have a tendency toward constipation. The attacks are apparently not precipitated by dietary indiscretion, but there is often a history of prolonged overeating without symptoms.

In many cases, no precipitating cause for the attack can be found. In many other cases, such a cause can be found, and is usually a nervous one. Unusual excitement or fatigue are the most common exciting causes, and an attack may be precipitated by fright, grief, anger, or a railroad journey, a children's party, anxiety or overwork at school, exposure to cold, or anesthesia with chloroform or ether. Sometimes a minor illness, such as tonsillitis, bronchitis, or an ordinary cold, seems to act as the precipitating cause.

Several epidemics of acidosis have been reported. In one epidemic in Birmingham, Ala., reported by Park, gastro-intestinal symptoms were prominent, and it is probable that in these cases the exciting cause was an intestinal infection. Another epidemic was reported by Metcalf, occurring in Concord, N. H., and vicinity. No definite evidence of an exciting cause was obtained in this epidemic, and it is probable that some unrecognized infection was responsible for the epidemic occurrence of the disease. Acidosis was unusually common around Boston in the winter of 1915 and 1916, but the type was apparently only symptomatic of a prevalent grippe-like infection of the upper air passages. In these epidemics the clinical type is not that of recurrent vomiting, but rather of a general intoxication.

SYMPTOMS.—There are two distinct clinical types seen in cases of acidosis. In the first type, vomiting is the principal symptom throughout the seizure, and the attacks of vomiting have a pronounced tendency to recur at intervals. In the second type, while vomiting is usually an early and marked symptom, it is not so prominent throughout the attack, the most important symptom being a pronounced intoxication affecting the nervous system. This type does not have a definite tendency toward recurrence. The distinction between these two types is purely clinical, and does not necessarily imply any difference in etiology. There may be a corresponding difference in etiology, but if so, it is not known. The distinction between these two types is not generally clearly drawn in pediatric literature, because both are characterized by the appearance of acetone bodies in the urine, and the second type is considered only as

a varying manifestation of acidosis. Nevertheless, the distinction is valuable, not only for purposes of clinical description, but also because the two types show a marked difference in prognosis, and in the indications for symptomatic treatment. The first type has usually been spoken of as recurrent, cyclic, or periodic vomiting, and will be described under that heading. The second type will be described as "acid intoxication," with the proviso that this term does not imply that the symptoms are due to the accumulated acids, but is only used for convenience of description.

RECURRENT VOMITING

(Cyclic Vomiting.). (Periodic Vomiting.)

The attack is very apt to come on suddenly, the child having been previously in good health, and not having shown any digestive disturbance. At times, prodromata have been observed, the most common being languor, pallor, irritability, easy fatigue, restless sleep, coated tongue, anorexia, and constipation with stools that are either very light colored, or spongy and sour.

Whether or not there are premonitory symptoms, vomiting begins suddenly. The vomiting may be almost continuous, or may occur at intervals, usually of about fifteen minutes, but sometimes longer. The vomiting may be violent and projectile. After about twelve to twenty-four hours, it may become somewhat less frequent, but is still the principal symptom of the disease. The vomitus at first consists simply of the food which has been eaten, and after the stomach is empty, of mucus and serum. It may or may not have a sour odor, or the odor of acetone, and free hydrochloric acid may or may not be present. Later the vomitus often becomes streaked with blood, and occasionally, in untreated or in badly treated cases, considerable blood is vomited. Toward the end of the attack the vomitus is often bile stained. The vomiting is entirely uncontrollable, the stomach retaining nothing. Not only food, but all water, and any medicine given, are immediately vomited. The straining of the vomiting causes muscular lameness and tenderness of the abdomen, but there is no marked abdominal pain.

Thirst is always a prominent symptom, the child crying continually for water. Anorexia is usually very marked. Restlessness is usually great in the early stages of the attack, but later the patients appear to be afraid to move or to talk lest vomiting be provoked. The bowels are usually constipated, the stools being light colored and offensive.

The temperature in this type is rarely much elevated. It is ordinarily under 100.5° F. even at the onset, and later it is usually normal or subnormal. The pulse is often slow at the onset, but later becomes

rapid, weak, and sometimes irregular. The respiration is usually little if at all disturbed in this type; it is occasionally somewhat shallow and irregular. The tongue is ordinarily dry and coated, sometimes cracked, and the lips are dry and parched. The breath often has the odor of acetone strongly marked, but this cannot always be detected. The abdomen is usually retracted, and the skin may be dry and harsh, or cold and clammy.

During the first twenty-four hours the appearance of the child is not markedly altered. After this time emaciation is rapid, the child has a sunken-eyed appearance, looks severely ill, and prostration may become marked. Nevertheless, in this type, delirium, stupor and coma do not occur. The patient may be somewhat apathetic, but is always acutely conscious of his surroundings, and usually answers questions promptly and intelligently. In fact, the mental condition seems clear in comparison with the severity of the vomiting, and with the degree of prostration.

The urine is scanty and concentrated, but with proper treatment it may be more profuse. Toward the crisis of the attack its secretion becomes abundant, and this may be the first sign of improvement. It is strongly acid. The test for acetone usually gives a strongly positive result from the very start of the attack, and I have seen the sudden appearance of acetone precede the attack by twelve hours. The acetone test remains strongly positive until the crisis of the attack, when it becomes gradually less marked, disappearing in a few days. The test for diacetic acid is usually, but not always, positive from the start of the attack, and persists till the crisis is approached. Diacetic acid usually disappears from the urine before the acetone. The urine also contains an excess of indican, uric acid, creatin, the xanthin bodies, and sometimes beta-oxybutyric acid. During the height of the attack it may contain a trace of albumin, a few casts, and blood cells. The blood usually shows a moderate leukocytosis.

The duration of an attack is absolutely variable. It may be only a few hours, or it may be a week or even more. The most common duration is from two to four days. There is, however, a gradual tendency toward an eventual shortening of the duration of the successive recurrent attacks. The severity of the attacks is just as variable. This marked variation in the duration and severity of the attacks makes any opinion as to the value of any method of treatment in shortening the attacks, absolutely inconclusive and worthless.

The attacks recur at intervals, without any definite or obvious exciting cause. The intervals between the attacks are absolutely variable in length. The seizures may occur every week or two, or only after intervals of a number of months. In general, the

intervals tend to become longer as the patient grows older, but there are many irregularities, and several attacks may occur at short intervals after a long period of freedom. The length of time during which the tendency toward recurrence persists is also absolutely variable. The recurrences may continue throughout childhood, or may cease at any time. This variation in the intervals between attacks, and in the general duration of the disease, makes any opinion as to the value of any prophylactic treatment, or treatment in the interval, absolutely inconclusive and worthless.

The attacks in recurrent vomiting usually terminate by crisis. Within a period of twelve hours, usually, the paroxysms of vomiting become less frequent with longer intervals of sleep, and then cease for good. The other symptoms disappear rapidly, and appetite and normal digestion return almost at once. Convalescence is remarkably rapid, and within a few days the child is as well as ever.

“ ACID INTOXICATION ”

(Acidosis.)

This type is often spoken of as acidosis in distinction to recurrent vomiting, but many writers make no distinction. It is more frequent in infants than in later childhood, the commonest period being between one and three years. It is the type associated with the reported epidemics of acidosis. It is much more dangerous than recurrent vomiting, and does not tend to recur at intervals, although in the Concord epidemic some cases were seen in children who had had recurrent attacks.

The onset in this type is in every way similar to that of recurrent vomiting. It may be sudden, or preceded by the same prodromata. The first symptom is severe and uncontrollable vomiting. The acetone odor in the breath and the early appearance of the acetone bodies in the urine, are both present. In the first twelve or twenty-four hours, there is little to distinguish the case from the more common recurrent type. The temperature, however, is apt to be more elevated, often reaching 102° F., 103° F., or even more. There is also sometimes evidence of intestinal disturbance, as shown by diarrhea.

After this initial period of twelve to twenty-four hours, the vomiting becomes less frequent and severe. Everything taken by mouth is not immediately vomited, and while vomiting takes place at intervals, water and food are usually retained for a considerable period.

The essential clinical feature of this type is, that with the improvement in the vomiting, the general condition of the patient does not improve. Apathy becomes more marked, although wasting is often not so rapid. The patients finally become drowsy, and react

very sluggishly to their surroundings, and may become increasingly more stuporous. Delirium may be present, and occasionally convulsions.

With the increasing clouding of the mentality, there is usually a notable disturbance of respiration. In typical cases, the special dyspnea of air hunger is present.

The patient lies with the eyes half closed, with the eyeballs partly rolled up, and the conjunctivae injected. The lips are often of a peculiar cherry-red color. In severe cases prostration becomes very marked, and the patient sinks into coma, while the vomiting often ceases altogether. In fatal cases the pulse becomes gradually more weak and rapid, the respiration more rapid and shallow, the temperature rises to 105° , 106° , or even higher, and death occurs in coma.

In milder cases the drowsiness gradually passes off, and the vomiting ceases, but recovery is less abrupt than in the recurrent type, and the acetone bodies often do not disappear from the urine for a number of days. After recovery, a second attack is very exceptional.

DIAGNOSIS.—The problems presented in diagnosis in the first attack of recurrent vomiting, and in the early stage of the toxic type, are the same. The conditions to be particularly considered are, acute indigestion, the onset of an acute infection such as scarlet fever or meningitis, appendicitis, intussusception, and tuberculous meningitis.

ACUTE INDIGESTION.—It is often difficult to distinguish acidosis from acute indigestion in the first twenty-four hours, vomiting being often the only symptom of both conditions. If the urine can be examined early in the attack, there will be a very strong acetone reaction in acidosis, and a slight or absent reaction in indigestion. Later, acetone may be present in indigestion with vomiting, but a very marked reaction points toward acidosis. Moreover, in indigestion, after the stomach is emptied of food, the vomiting usually occurs only after the giving of food. Everything taken is vomited, but there is not the continual retching characteristic of cyclic vomiting. Also, in indigestion, water is not often vomited, while it is almost always vomited in acidosis. These distinctions, however, are not always clearly marked, and the final test is the response to treatment. The vomiting of indigestion usually ceases with proper treatment, while that of acidosis continues irrespective of treatment.

ACUTE INFECTIONS.—A number of acute infections in childhood begin with vomiting at times. In particular, vomiting is often a prominent symptom of scarlet fever and meningitis. The diagnosis depends mainly on the results of a careful physical examination, which will often disclose the characteristic signs of the infection of

which the vomiting is a symptom. The presence of high fever is in favor of some acute infection; it is strongly against the recurrent type of acidosis, but does not rule out the other type, although the fever in acute infection is higher as a rule than in any form of acidosis. The examination of the urine for the acetone bodies is of help, if made early in the attack. The early presence of a marked acetone reaction points toward acidosis. It must be remembered, however, that the appearance of the acetone bodies in the urine is a frequent symptom in many acute infections, and acetone is likely to be present in any case in which vomiting has continued a number of hours. It is therefore very important not to conclude too hastily from the presence of acetone that the case is one of the so-called primary types of acidosis. Such a conclusion may lead to carelessness in physical examination, and to the overlooking of any signs of a recognizable acute infection which may develop in the course of the disease.

In general, when uncontrollable vomiting is the principal symptom, if the temperature is not much elevated, and if the urine shows a strong acetone reaction, it is safest to consider and treat the case as one of acidosis, while watching carefully for signs of some other disease. If the temperature is high from the start, it is safer to consider the case one of acute infection until characteristic signs of the infection fail to develop, or until signs of the toxic type of acidosis begin to appear. If, however, the acetone bodies are present in the urine, it is safe to use the treatment for acidosis, as this can do no harm if the acidosis be secondary and symptomatic rather than one of the primary types.

APPENDICITIS.—I have frequently seen appendicitis mistaken for acidosis, and have myself mistaken acidosis for appendicitis. The first mistake is due to the fact that with the increase in the use of accurate laboratory methods of diagnosis, physicians are apt to overemphasize the results of a laboratory examination, and to underestimate the importance of careful and thorough physical examination. In appendicitis, severe vomiting and acetonuria are common symptoms, and if the physician finds that the examination of the urine gives a positive test for acetone, and jumps at the conclusion that the case is one of acidosis, there is danger that he may neglect the careful physical examination necessary to reveal the presence of appendicitis in early life. In acidosis, while tenderness of the abdomen is usually absent, it may be present from the soreness of the muscles of the abdominal wall which often follows excessive vomiting. Appendicitis can only be ruled out when its characteristic signs, such as paroxysmal pain, abdominal tenderness and spasm, are all absent. When any of these signs are present, the differential

diagnosis may be quite difficult. The physician must take everything into consideration. Fever, localized tenderness, paroxysmal pain, a marked leukocytosis, and the retention by the stomach of some food or water, favor appendicitis. The absence of these signs, with a strong acetone reaction in the urine, favors acidosis.

INTUSSUSCEPTION.—This is another condition of which vomiting is a prominent symptom, and in which acetone may sometimes be found in the urine. It is distinguished from a primary acidosis by the appearance of the characteristic bloody discharges, and by the finding of a tumor on careful physical examination.

TUBERCULOUS MENINGITIS.—This condition is the one which presents the greatest difficulties in the differential diagnosis from acidosis. Severe vomiting is a common symptom in the early stages of tuberculous meningitis. If at this time the examination of the urine for acetone be negative, acidosis may be ruled out, and some other cause must be sought for the vomiting. While acetonuria is less common in tuberculous meningitis than in other acute infections, it may appear in any child who has been vomiting for some time. Consequently even in the early stages of either type of acidosis, tuberculous meningitis cannot be excluded with certainty. With the presence of a marked acetonuria, however, it is best to treat such cases as acidosis, because if the disease later proves to be tuberculous meningitis, no harm has been done.

In the further course of the two conditions, certain differences often appear. In the recurrent type of acidosis, vomiting continues to be the principal symptom, and continues to be uncontrollable, the stomach rejecting everything taken. In tuberculous meningitis, the vomiting is apt to be less severe, and often some food or water is retained. The abrupt cessation of the vomiting in the recurrent type of acidosis is accompanied by a favorable change in the condition of the child, and this distinguishes this condition from tuberculous meningitis, in which improvement in the vomiting is not attended by improvement in the general condition of the child. In the later stages it is very difficult to distinguish the second type of acidosis from tuberculous meningitis, because both diseases are characterized by clouding of the mentality. In this stage of tuberculous meningitis, however, when the vomiting remits, the acetone reaction is likely to disappear from the urine, while in acidosis, it continues to be marked. It is nevertheless often difficult to make a differential diagnosis in all stages of the disease, except by lumbar puncture. I believe that in any case in which the diagnosis lies between acidosis and tuberculous meningitis, lumbar puncture should be performed. It is true that if the case be one of tuberculous meningitis, the lumbar puncture does no good; but it is also true that if

the case be one of acidosis, lumbar puncture will do no harm. The advantage to be gained for purposes of prognosis and treatment in thus settling the diagnosis is very great. In acidosis as in tuberculous meningitis, the cerebro-spinal fluid is clear, and it may even be under increased tension. The cell count of the cerebro-spinal fluid, however, is usually normal in acidosis, while in tuberculous meningitis it is invariably increased. Rarely cases of the toxic type of acidosis will show some increase in the cell count of the cerebro-spinal fluid, but this is usually moderate and much less than the usual cell count of tuberculous meningitis. The finding of the tubercle bacillus in the cerebro-spinal fluid is always positive evidence.

PROGNOSIS.—In recurrent vomiting the prognosis is in general favorable. A fatal ending is rare in this type. Cases have been reported in which death occurred as a result of extreme prostration in recurrent vomiting, but such cases are certainly rare. I have only seen two fatal cases in this type of acidosis. Both had been improperly treated and were characterized by the vomiting of large amounts of blood. I believe that this is the chief danger in recurrent vomiting. The continual retching seems to cause a mechanical injury to the mucous membrane of the stomach, leading to hemorrhage. The toxemia of the disease is certainly very rarely a cause of death. In the first attack, the prognosis is somewhat more doubtful, because the physician cannot tell at the start whether he has to do with the recurrent type, or the "acid intoxication" type. So long as no clouding of the mentality develops, the outlook is good. In subsequent attacks a favorable prognosis can be given in any case in which the vomiting of considerable blood has not already developed.

In the type of acidosis characterized by clouded mentality, stupor, or coma, the prognosis is much more unfavorable. Such cases are often fatal, particularly in infants, and the younger the child the worse the prognosis. The prognosis varies with the severity of the case, and this is measured by the degree of stupor which develops. If the infant's symptoms do not advance beyond apathy and slight clouding of the mentality, the prognosis is good, for the disease is a self-limited one. When marked stupor or coma develop, with disturbance of the respiration, the prognosis is very bad. In a child under two years, the chances are rather against recovery in any case of acidosis of this type.

TREATMENT. RECURRENT VOMITING.—The treatment of recurrent vomiting may be subdivided into that of the acute attack, and that of the interval.

In an acute attack of recurrent vomiting, the chief danger comes from the vomiting itself. Excessive vomiting may produce hemor-

rhage, or may cause severe exhaustion and prostration, which is increased by the deprivation of food and fluid. The chief indications therefore, are to diminish the frequency and severity of the vomiting, and to supply as much fluid and fuel as is possible.

The essential measure to be used for the excessive vomiting is to *give no food, fluid or medicine by mouth* until the attack ceases. This has more effect in diminishing the frequency and severity of the vomiting than any drug, or any other measure. Once that the diagnosis of recurrent vomiting is made, allow nothing to pass the child's throat. Do not give bicarbonate of soda, do not give aerated water, iced brandy or champagne, do not give cracked ice to be melted in the mouth. Every drop of fluid which enters the stomach will provoke vomiting, but if nothing enters, the vomiting will certainly decrease in frequency or severity. No drug is of any marked value in controlling the vomiting. The value of bicarbonate of soda as a specific weapon against acidosis will be considered later, but it is certainly not great enough to warrant its being given by mouth in the recurrent type of acidosis.

From the beginning of the attack, *the child should be put on rectal feeding*. Children can usually be satisfactorily nourished in this way during the comparatively short duration of an attack of cyclic vomiting. It is often surprising to see the favorable change which takes place in a child with whom feeding by mouth has previously been tried, when rectal feeding is instituted. Much of the prostration disappears, the sunken-eyed appearance improves, emaciation becomes less rapid, and the pulse becomes of better quality. These changes come from the much needed supply of food and fuel, which cannot be retained by the stomach, but which are usually readily retained and absorbed by the rectum.

The best food for use in the nutrient enemata is dextrose. It is the only food substance which can be given in the same form in which it is absorbed into the blood and utilized by the tissues. It is fortunately a carbohydrate, and as acidosis most probably involves a disturbance of the glycogenic function of the liver, with a consequent insufficient supply of sugar, this form of fuel is the one needed. Pure dextrose is expensive, and cannot always be readily obtained. Glucose is the next best substitute. If neither can be obtained at once, peptonized milk may be used during the interim, but is theoretically greatly inferior to dextrose.

The dextrose should be given in a 5% solution. More dextrose could be given in a stronger solution, but there is danger of irritation of the mucous membrane, and of intolerance of the rectum, which should be avoided at all costs. The amount to be given at each injection depends on the age of the child, and the tolerance of the rectum. It is safer to begin with a smaller amount, and later to

increase the quantity. To an infant, four ounces every four hours should be given (1.2 oz. dextrose in 24 hours). To an older child, six ounces every four hours should be given (1.8 oz. dextrose in 24 hours). If the rectum seems tolerant, and these enemata are well retained, the quantities may be increased to six and eight ounces respectively. If they are not well retained, the quantities must be somewhat reduced. A cleansing enema should be given every twenty-four hours.

If, in spite of the nutrient enemata, the child complains of excessive thirst, normal saline solution should be given by rectum during the intervals between the nutrient enemata. The amount at each injection should be from two to four ounces, and the frequency should depend on the thirst of the patient, enough being given to relieve this symptom.

The majority of writers advocate the use of bicarbonate of soda in recurrent vomiting. This is based on the theory that the disease being apparently an acidosis, an alkali is indicated to counteract the excessive acidity of the blood. As I have shown in considering the etiology of acidosis, there is considerable evidence against the theory that the toxic symptoms are directly due to the accumulation of the acetone bodies in the blood. The vomiting may be due to other toxic products of disturbed metabolism, the acidosis being only an accompanying symptom, or, even if the symptoms are due to toxic acids, there is no proof that the accumulation of acids can be effectively combatted by the administration of bicarbonate of soda. There would be no objection to the use of bicarbonate of soda, if its administration could do no harm. In as far as the giving of bicarbonate of soda by mouth is concerned, I believe that it certainly does do harm by increasing the vomiting, and that the possibility of harm is greater than the possibility of good. Bicarbonate of soda, however, can be given in the rectal enemata. Here also I believe that it can have a harmful effect, in rendering the rectum so intolerant that the nutrient injections are not retained. In recurrent vomiting, the chief danger comes from the vomiting itself, and our most effective weapon against this symptom is rectal feeding. If the rectum becomes intolerant, the proper treatment of the case becomes very difficult. The question arises whether the benefit to be expected from the counteracting effect of bicarbonate of soda is sufficiently great, to balance the possibility of harm. In my opinion the evidence of benefit is not sufficiently great. In view of the variability of the clinical course in recurrent vomiting, and the tendency of the vomiting to *cease abruptly at any stage without reference to treatment*, reports on the apparent favorable action of bicarbonate of soda cannot be accepted as conclusive. Even if the urine becomes alkaline with bicarbonate of soda treatment *before* the vomiting

ceases, it is not conclusive evidence, because the urine often becomes alkaline as the crisis approaches without bicarbonate of soda treatment. I formerly used the bicarbonate of soda treatment first by mouth, in various quantities including the very frequent administration of a saturated solution, and later by rectum. I have never seen any clear evidence of its value. The disease is self-limited, and the attack will run a favorable course, if the vomiting is not excessive, and if the patient can be nourished and supplied with sufficient fluid. I do not, therefore, advocate the use of bicarbonate of soda in recurrent vomiting. In a very severe case, in which it seemed necessary to try every available resource for saving the life of the patient, bicarbonate of soda would be a possible measure, but in such a case, I would give it intravenously.

Under the routine treatment of no food by mouth, and dextrose and fluid by rectum, most cases will run a course without severe prostration, hemorrhage, or other unfavorable symptoms. Some cases, however, are more severe, and require additional treatment. Unfavorable signs are continued frequent and violent retching, with increasing prostration, or increasing blood in the vomitus. In such a case, ten grains of sodium bromide should be given by rectum, and if this does not lessen the vomiting, it may be repeated in two hours, with one and one-half to two grains of chloral hydrate. Subsequently the bromide may be given by rectum every four hours, if the vomiting continues to be severe. Morphin should not be used, except in the most desperate cases which resist the bromide. It seems to increase the toxemia of the disease, but should be tried if all other resources fail.

With very severe prostration, and a weak and rapid or intermittent pulse, the usual circulatory stimulants, caffeine, strychnin, and digitalis, should be used, given subcutaneously.

If the rectum becomes intolerant, the quantity of fluid given by rectum must be reduced, and only the dextrose should be given. Under these circumstances, physiological salt solution should be given subcutaneously, in doses of four ounces repeated as often as is necessary to control thirst. Dextrose solution, or a weak solution of sodium bicarbonate, may also be tried by mouth, under these circumstances.

When the vomiting has stopped for six or more hours, it is usually a signal that the attack is over, and that feeding by mouth may be begun. It is best to begin with a five per cent dextrose solution in barley water, beginning with teaspoonful doses, and doubling the amount every two hours. The nutrient enemata should be continued for twelve hours, or until eight ounces of the dextrose-barley solution are taken, when they can be omitted. Zwieback, or dry bread crust can now be added to the diet, or even before the expira-

tion of twelve hours, if the child's appetite returns rapidly. Cereals are added during the next twelve hours, and then milk may be given. After this the child can rapidly return to its normal diet.

Next must be considered the treatment of the child subject to recurrent vomiting, in the intervals between the attacks. According to the theories outlined above, prophylactic treatment should aim at the prevention of the absorption of the products of intestinal putrefaction, the removal of chronic foci of infection, the prevention of nervous excitement or fatigue, and the avoidance of dietary indiscretions.

Many writers claim remarkably good results in recurrent vomiting from dietetic treatment. Unfortunately, clinical observation cannot be accepted as a satisfactory criterion of the efficacy of any dietary regimen, on account of the variability of clinical course which is an essential feature of the disease. Dietary treatment is usually advocated on a basis of some exclusive theory of etiology, while the facts suggest a diverse etiology. For instance, if the theory be accepted that the absorption of putrefactive products from the intestine damages the metabolic functions of the liver, the protein in the diet should be reduced. On the other hand, if the theory be accepted that an excess of food beyond the oxidizing power of the child is the cause of the disturbance, it is the fats and carbohydrate, with their high carbon content, which should be reduced. In view of the obscurity which still surrounds the etiology of the disease, it does not seem that any exclusive theory can be logically adopted as a basis for dietary treatment.

I believe that *the principal thing to be avoided is overfeeding*. The diet should be arranged according to the ordinary principles which govern the selection of the food for the normal child of the same age. A well-balanced diet, with a proper ratio between fat, carbohydrate, and protein, should be insisted upon. In one respect, I agree with those who favor reducing the carbon content of the food, and that is in the advisability of omitting sugar from the diet. Sugar is not a necessary ingredient of the diet of children, and indeed before the last three centuries, was only used as a condiment, not as a food. Cane sugar is a common source of a form of intestinal fermentation, which is very insidious and difficult of clinical recognition. All the carbohydrate needed can be supplied from the starchy foods which make up an ordinary, well-balanced diet. I believe that an excessive amount of milk should be avoided, and that cream had better not be given. All eating between meals should be strictly forbidden.

With a normal, well-regulated diet, the stools should be frequently examined for evidences of fermentation, or for indigestion of any particular food element. If any such indications are found, the diet

should be modified accordingly. If the stools suggest fermentation, lactic acid milk should be tried.

It is essential that a satisfactory daily evacuation of the bowels be insured by suitable measures.

Adenoids or diseased tonsils, if present, should be removed, and if the child be subject to attacks of infection of the upper respiratory passages, a change of climate is advisable. Every possible focus of chronic infection should be diligently sought.

The treatment of the nervous system must be carefully attended to. All such possible precipitating causes as emotional excitement and nervous fatigue should be prevented by careful attention to detail. Some children must be taken out of school. Sometimes a change of nurse or other attendant, or even the temporary absence of the mother, is of benefit. Rest in bed in the morning or afternoon, or both, is sometimes advisable.

The evidence in favor of the value of any form of medication in the intervals between the attacks of recurrent vomiting can only be of the inconclusive clinical variety. The physician may freely indulge his fancy, provided that nothing be given that can do harm. The disease is of such a character that whatever he uses, he is likely to be convinced that he is obtaining "good results." Personally, I have no suggestions to offer.

The question of whether in a child showing recognizable prodromata, the attack can be aborted by medication, is an open one. I cannot declare that it cannot be so aborted. Many writers have claimed that the giving of bicarbonate of soda upon the appearance of prodromata will sometimes abort the attack. I have seen cases in which I believed that I recognized prodromata, and have given bicarbonate of soda, and no attack occurred. On the other hand, I have seen cases in which I believed that I recognized prodromata, and have *not* given bicarbonate of soda, also proceed without an attack. Prodromata in recurrent vomiting are indefinite and uncertain. Certainly, when given at this stage, before vomiting has begun, the giving of bicarbonate of soda by mouth is not open to the objections which prohibit its use during the attack. It may be given in doses of ten to thirty grains every two hours until the urine becomes strongly alkaline, and then enough should be given to keep the urine alkaline.

It is also advisable, upon the recognition of prodromata, to induce free catharsis, and to reduce the amount of food.

ACID INTOXICATION.—The treatment of the type of acidosis in which clouding of the mentality, stupor, or coma becomes the prominent symptom, is at first exactly like that of recurrent vomiting. Food or water by mouth should be interdicted, and the rectal ad-

ministration of dextrose and fluid should be instituted, and should be continued as long as vomiting is severe and uncontrollable.

When the development of clouded sensorium or stupor shows that the case is of the second type of acidosis, the indications for treatment undergo a marked change. We have now to do with a disease in which the danger comes, not from the vomiting, but from a pronounced intoxication affecting the nervous system, and tending toward coma and death. The only specific measure for combatting this intoxication which possesses any theoretical basis, is the administration of bicarbonate of soda. Whether or not it is effective is an open question. At all events, it is the only thing which can be done, and should therefore be employed. Usually in this type, after the symptoms have developed, the vomiting is not so severe. A considerable amount of bicarbonate of soda can usually be retained by mouth, and if any be retained, occasional vomiting is not a contraindication. As much bicarbonate of soda as possible should be given, usually from ten to thirty grains every two hours to an infant, and even more to older children. Often children take and retain it better when given in dry form instead of in solution. If the soda can be given by mouth, it is best not to give it by rectum, in order not to injure the tolerance of the rectum for the necessary food and fluid. If the soda is not well retained by mouth, it may be tried by rectum, and the giving of small amounts of dextrose solution in barley water by mouth should be tried. Either the mouth or the rectum should be used for the soda, but not both at once.

If under this treatment, the case continues to run an unfavorable course, the bicarbonate of soda may be given intravenously. From sixty to ninety grains (4-6 grammes) should be given in four to eight ounces of water according to the age of the child. In infants, the technique of intravenous injections is very simple, owing to the easy access to the longitudinal sinus through the open fontanelle. In older children, some other vein must be chosen.

My personal experience with the bicarbonate of soda treatment has not been very encouraging. I have given it intravenously in large doses without effect on either the symptoms or the acidity of the urine, and then, two or three days later, the symptoms have improved and the urine has become alkaline spontaneously.

The other measures of treatment, such as stimulation, are the same in this type as in an attack of recurrent vomiting. Physiological salt solution subcutaneously is a valuable stimulant. In convalescence, the feeding is conducted along the same lines as recurrent vomiting, the rectal feeding not being omitted until sufficient food and fluid can be taken by mouth.

PROBLEMS AND RESEARCH.—The problems of acidosis are chiefly connected with the cause of the condition, and have been indicated in the discussion of the etiology. The fundamental problem is whether there is a primary acidosis with a specific cause, or whether the disturbance of metabolism which results in acidosis is always a secondary symptom-complex of some other pathological condition. It is probable that the increasing study of some of the more obscure infections will relegate to the secondary class many cases of acidosis now considered primary. It is probable also that the progress of research on the subject of the metabolism in early life will result in the subject of acidosis in children being attacked with the same thoroughness as has diabetes mellitus in adults. This is likely to throw much additional light on the subject, and may also result in revealing the secondary character of acidosis. It is very probable that the types of acidosis which are not recurrent, and which sometimes occur in epidemics, will eventually be classified as secondary symptom-complexes, when the causes are more fully understood. As for the recurrent vomiting type, while this also may prove to be a secondary manifestation, the definiteness of the clinical picture is strongly suggestive of some specific form of metabolic disturbance.

Other problems are the relation of the acetone bodies to the symptoms, the nature of any other toxins which may be the cause of the symptoms, and the exact character of the disturbance of metabolism which results in the excessive formation of the acetone bodies and other toxins. For a solution of these problems we must await further progress in the complicated subject of the chemistry of metabolism.

The problems are being attacked by modern methods. Improved methods of studying the acidity and chemistry of the blood are being published. The method of studying acidosis by the estimation of the carbon dioxide content of the alveolar air has thrown much light on the relative form of acidosis, but has not yet been extensively applied to positive acidosis. Howland is at present doing much work on acidosis.

As an example of the methods now being employed, I note a recent publication of Marriott, describing an improved method of estimating quantitatively the acetone bodies in the blood. He found no fixed relation between the amount in the blood and the amount in the urine. There is also a recent work by Fischler and Kossow on the origin of the acetone bodies. This was an experimental study on dogs by means of Eck's fistula on the partially excluded liver, and showed that acetone, diacetic acid, and beta-oxybutyric acid, are mainly formed in the liver. This method of investigation seems very promising.

DIABETES MELLITUS

Diabetes mellitus is a disorder of metabolism characterized by the accumulation of grape-sugar in the blood, and by its excretion in the urine over long periods. It is a rare disease in childhood as compared with adult life, but is not so rare as was formerly supposed. An increased number of cases of diabetes mellitus have been reported in the last ten years, and this is probably due, not to an increased frequency of occurrence, but to better recognition of the disease. According to most statistics, only from .5 to 1 per cent of all cases of diabetes mellitus occur in the first ten years of life. Van Noorden's statistics show the incidence for the first decade to be 2.5 per cent, and it is probable that the average incidence is about 2 per cent.

ETIOLOGY.—Diabetes mellitus can occur at any age. It is probably extremely rare in infants. Knox found but seven cases in infants under one year reported in the forty-four years between 1852 and 1896, while it has been described in at least nine babies in the fifteen years between 1896 and 1913. The frequency of the disease in childhood apparently increases directly with the age. The frequency of occurrence of diabetes mellitus in early life cannot be accurately estimated, because many cases have undoubtedly been overlooked, owing to the difficulty of obtaining urine from young children, while on the other hand, diabetes mellitus is often falsely diagnosed, owing to the tendency of young children to excrete milk-sugar and other reducing bodies in the urine, and to exhibit a transitory glycosuria.

The preponderance of male diabetics seen in adult statistics does not hold for childhood. The two sexes appear to be affected with about equal frequency in the diabetes of early life. The influence of race is also not so apparent in childhood as in adult life, the Jewish race not showing so marked a predisposition towards diabetes mellitus in childhood.

Heredity is an important factor in the etiology of diabetes mellitus. There are many recorded instances of diabetes in children having a diabetic family history, but the influence of heredity is not so evident in childhood as in adult life. Close investigation of the family history has often shown that the parents of diabetic children were blood-relatives, or that intermarriage occurred in former generations. This is strongly suggestive that diabetes in children is an endogenous degenerative disease. Syphilis in the father has sometimes been recorded, suggesting the possibility of a functional weakness of the pancreas from the syphilitic virus.

The immediately exciting cause of diabetes mellitus which has been most frequently described, is an injury to the central nervous system. Such injuries have come from trauma, as in falls, blows,

or as the result of difficult labor, or from disease or deformity of the brain. The relation of these injuries to the disease is a subject of present day discussion, some authorities believing that diabetes can have a neurogenous origin independently of the pancreas, while others believe that an injury to the nervous system acts by affecting the pancreas. (Von Noorden.)

Diabetes mellitus in children sometimes appears to follow the consumption over a long period of an excessive quantity of sugar.

The general etiology, the pathogenesis, and the abnormalities of metabolism in diabetes mellitus have aroused great interest in recent years, and have been the subject of much experimental investigation. Owing to the rarity of the disease in early life, this is not the place for a lengthy consideration of these subjects, and the reader is referred to the works which consider the disease in adults, and to the voluminous special literature of the subject. A brief summary of the newer teaching concerning the disease may, however, be useful and interesting to those who have not followed the recent literature. Such a summary will be found under the heading of problems and research.

PATHOLOGICAL ANATOMY.—Diabetes mellitus shows no constant characteristic lesions. In a certain number of cases, some lesion of the central nervous system, either developmental, or the result of trauma, or from acquired disease, has been found. In many cases there is no lesion of the nervous system.

In the last two decades, increasing attention has been paid to the pancreas. In the older autopsies the condition of this organ was usually not recorded, while in more recent records there is frequent mention of a small size and shrunken condition of the organ. A diminution in the number of the islands of Langerhans has been often recorded of late, and some authorities believe that a careful count of the number of islets in a given area will often if not always show such a diminution in diabetes.

SYMPTOMS.—The chief symptoms of diabetes mellitus are the same in children as in adults, namely increase in the secretion of urine, excessive thirst and hunger. The onset of the disease has generally been described as much more rapid and sudden in children than in adults. This is probably not markedly the case, but the disease has appeared to come more suddenly, because it has not been recognized in its early stages. The urine of children is not examined as often as that of adults, and symptoms in children in the early stage are not pronounced, and consequently the disease is not recognized until marked symptoms have betrayed the existence of the disease which appears to be already in a severe stage. Nevertheless, it is probable that acute types are met with in childhood more often than in adult life.

The first symptom in children is usually *enuresis*, and no case of enuresis should be allowed to pass without examination of the urine for sugar. In some cases the *excessive thirst* is the first symptom which attracts attention; in other cases it is *flecks of sugar* on the child's underclothes. *Irritation of the external genitals* is a fairly common symptom in childhood, and should always lead to a urinary examination. Excessive hunger is a rare symptom, but is rather more common in children than in adults. The various complications, such as disorders of the skin, eyes, and nervous system, which so frequently cause the first suspicion in adults, are almost unknown in childhood. Sometimes, however, a marked change in the child's disposition is observed.

When the disease is recognized in an early stage, before the tolerance for carbohydrate fails, regulation of the diet will usually bring about a disappearance of all symptoms, including the glycosuria. Whenever, during this period, an increased quantity of carbohydrate is given, sugar will reappear in the urine. During this mild stage, the physical and mental development of the child is normal. The duration of this stage is very variable; it may be weeks, months, or even years.

Sooner or later the tolerance for carbohydrate fails. The failure may be precipitated by some intercurrent febrile disease or by a dietary indiscretion, but even in the absence of such causes, it is only postponed, and inevitably occurs in the course of time. When once the carbohydrate tolerance begins to diminish, the development of complete failure, with a severe type of glycosuria unmodified by carbohydrate withdrawal, is very rapid. With the loss of tolerance, symptoms develop. The patients lose physical and mental activity, tire easily, and complain of pain in the joints after exertion. Polyuria, excessive thirst, and sometimes excessive hunger become prominent, and emaciation is very rapid.

Even at this stage a carefully arranged dietary may cause some improvement in the symptoms, but the improvement is only temporary. With the rapid emaciation, the acetone bodies appear in the urine, the breath has the odor of acetone, and the patient presents the same picture of acid intoxication as is seen in adults.

Unless some intercurrent infectious disease occurs, the termination of diabetes mellitus in children is death in coma. The approach of diabetic coma is often indicated by such symptoms as loss of appetite, nausea, vomiting, gastric pain, nervous irritability, sleeplessness, and muscular weakness.

The urine in children shows the same abnormalities as in adults. During the mild stage, sugar (dextrose) is constantly present on a normal diet, or when the carbohydrate in the food is increased, and the quantity and specific gravity are proportionately raised. Under

dietary regulation, the sugar disappears. In the severe stage, the quantity of urine excreted in twenty-four hours is increased to from two to four times the normal, and the specific gravity is increased up to 1040 or even more. Sugar is constantly present, varying in amount up to 60 grammes or even more in twenty-four hours. The urine contains varying amounts, first of acetone, later of diacetic and oxybutyric acids, and large amounts of ammonia. There is usually a trace of albumin, and as coma approaches, an increasing number of the small, so-called "coma casts," are seen in the sediment.

The complicating organic diseases so common in the diabetes of adult life are almost never seen in the diabetes of childhood.

DIAGNOSIS.—The diagnosis of diabetes mellitus in children, as in adults, depends upon the finding in the urine of the constant presence of dextrose, when the patient is on a normal diet. This is positive proof of the existence of the disease.

Diabetes in children is often overlooked, especially in the early stages, on account of the common neglect of urinary examinations. In all cases, such symptoms as enuresis, thirst, abnormal appetite, irritation of the external genitals, and wasting, should lead to urinary examination.

Diabetes mellitus is sometimes wrongly diagnosed, especially in infants. In a number of conditions in infancy, lactose, or the split product galactose, enters the circulation through the intestinal wall, and is excreted in the urine. With the ordinary test with Fehling's solution, lactose will give a reduction, and such a reduction has led to many errors in diagnosis. For the tests which distinguish dextrose from the other sugars, such as the phenylhydrazin test, the reader is referred to works on chemistry. A simple test for ordinary clinical use is the following: Boil the urine with an equal amount of a 10% solution of sodium hydrate for three minutes. Then add Fehling's solution and boil again. If the Fehling's solution is reduced, the sugar is lactose, not dextrose.

Another difficulty in diagnosis comes from transitory glycosurias, which are fairly common in children. Some children have a definite intolerance toward carbohydrate, which is not progressive in character. These cases are recognized by the fact that glycosuria does not occur with a normally balanced diet, but appears temporarily after the eating of an excessive quantity of carbohydrate. The finding of sugar in a single specimen of urine should never be considered evidence enough to warrant a diagnosis of diabetes. Only if the sugar is constantly present with a normal diet, or if intolerance as shown by glycosuria toward an excess of carbohydrate is increasing, should diabetes mellitus be diagnosed. Rare cases have also been reported of glycosuria in children, probably dependent upon

some transitory disorder of the pancreas, which disappears in a few weeks. Diabetes mellitus should be strongly suspected in such cases, but a positive diagnosis should not be made unless the glycosuria persists for a considerable time, or unless other symptoms of diabetes mellitus are present.

PROGNOSIS.—If the diagnosis of true diabetes be certain, the prognosis in children is almost without exception unfavorable. Practically the only hope for the child is that some form of transitory glycosuria is present. The lapse of time, or the progressive appearance of symptoms finally settles the point. After complete failure of carbohydrate tolerance occurs, progress toward a fatal ending is very rapid in children. Before complete failure occurs, the course of the disease is very variable in length.

TREATMENT.—In spite of the hopelessness of the prognosis, it is the physician's duty to prolong life as much as possible. The treatment is mainly dietary, and is conducted in the same way as in the diabetes of adults. Carbohydrate should first be gradually withdrawn from the diet until the urine becomes sugar-free, and then, by the gradual addition of a measured quantity of bread, or some other carbohydrate, the tolerance can be definitely determined. In mild cases, in which there is a definite carbohydrate tolerance, the diet should be carefully arranged in such a way that the carbohydrate given is within the limit of tolerance, with an occasional day of strict carbohydrate-free diet. The details of the arrangement of the diet depend upon the age, appetite, and powers of digestion of the individual child, and cannot be illustrated by definite schemata. The quantity of the protein should also be reduced if possible, but should not be below 2 grammes per kilogram of body weight. Usually the protein cannot be reduced as low as this, as the caloric value of the diet cannot be maintained by fat without indigestion, or by carbohydrate without overstepping the tolerance. The experience of many observers suggests that oatmeal is the form of carbohydrate best tolerated in the diabetes of children, although this has not been finally proven.

In infants, in whom the development of the digestive apparatus does not permit a varied diet, and whose food consists of milk, it is often difficult to determine the limits of carbohydrate tolerance on account of the quantity of lactose contained in all milk modifications. Carbohydrate can be greatly reduced, if not completely excluded, by the use of precipitated casein, either alone in a suspension, or in the form of albumin milk. With precipitated casein and top milk (16% cream) a formula can be arranged containing—Fat 2%,—Lactose .40%,—Protein 2.5%. (See Division on Feeding.) If with such a food glycosuria is present, the carbohydrate tolerance

may be considered to be practically zero. It may be accurately determined by gradually increasing the percentage of lactose in the food, and when this is determined, the formula may easily be arranged to meet the requirements.

When the tolerance for carbohydrate is zero, as shown by the presence of glycosuria when any carbohydrate is given, or when none is given, it is useless to continue strict dietary rules. A certain amount of carbohydrate, except cane-sugar, may now be given, either in the form of milk, or cereals. The so-called "oatmeal cure" of von Noorden may be tried. This consists in putting the patient for one or two weeks on a diet consisting of 150 grammes of oatmeal, 150 to 200 grammes of butter, and four or five eggs daily, and in addition, some wine. This sometimes shows a marvelous result in increasing the carbohydrate tolerance, but unfortunately, the improvement does not last.

No drug has any influence on the disease. When the acetone bodies are present in the urine, bicarbonate of soda should be given in doses of two to four drachms daily, to neutralize the acid products of the impaired metabolism. Some recent writers have advocated the use of the lactic acid bacillus (*bacillus bulgaricus*) in diabetes, on the theory that it diminishes intestinal putrefaction and the resulting autointoxication which disturbs the function of the pancreas, adrenals, thyroid, nervous system, and hypophysis. As lactic acid milk is low in carbohydrate content, this treatment might well be tried.

When diabetic coma occurs, the only measure which can even temporarily relieve the symptoms, is the intravenous injection of bicarbonate of soda. This has given good results in certain cases, but can only postpone the fatal termination.

PROBLEMS AND RESEARCH.—The following is a summary of the newer teaching as to diabetes mellitus:

Diabetes mellitus is a condition in which the liver shows an abnormal tendency to discharge dextrose into the blood in excess of the capacity of the tissues to utilize it. The hepatic function of dextrose formation from the stored glycogen is normally regulated by two factors, one stimulating, the other inhibitory. The stimulating factor lies in the chromaffin system of the adrenals, and this in turn may be stimulated by influences coming from the central nervous system. The inhibitory factor lies in the internal secretion of the pancreas, and this in turn is normally stimulated by the secretion of the parathyroids. The inhibitory action of the pancreatic secretion may also be *lessened* by disease of the pancreas, or by overactivity of the thyroid or hypophysis. Any influence which overstimulates discharge of sugar, or lessens the inhibition to dis-

charge of sugar, may theoretically produce diabetes mellitus. This explains the experimental production of diabetes through injury to the nervous system, and its occasional clinical association with such injury. Practically, however, von Noorden and his followers believe that the most important causes in human diabetes are those which lessen the inhibitory action of the pancreas, such as disease of the pancreas, and disorders of the organs which influence the pancreatic function. Whatever the ultimate cause, there is in all cases of diabetes an abnormal irritability of the dextrose-forming mechanism of the liver. The rational treatment of diabetes consequently consists in efforts to calm this excessive irritability by the avoidance of stimulation. The taking of sugar acts as a stimulus to the glycogenic function of the liver, and it is for this reason that the carbohydrates are to be so limited as to lie within the tolerance of the individual, as shown by absence of glycosuria. There is evidence that under certain circumstances the proteins may act as stimulants to the liver cells, but the fats are not excitants. The protein, however, cannot be kept low too long. Acidosis and diabetic coma are the result of an insufficient supply of carbohydrate. The success in some cases of the "oatmeal cures" suggests that some forms of carbohydrate stimulate the discharge of dextrose less than others. If this is so, the reason is unknown. Some recent writers believe that there is no special value in oatmeal, having obtained equally good results with wheat flour. This is explained on the theory that the good results come from the use of a single variety of carbohydrate rather than from a special variety, the use of a single variety allowing an increased tolerance to take place in the same way that tolerance for a drug is increased.

DIABETES INSIPIDUS

Diabetes Insipidus was described by Johann Peter Frank in 1794 as "a long continued, abnormally increased, secretion of non-saccharine urine which is not caused by a diseased condition of the kidney." This original definition still holds good. The disease is much less common than diabetes mellitus, its occurrence being about 14 per 100,000 dispensary cases. It is less common than diabetes mellitus even in childhood, although more common in proportion to the total number of cases at all ages. About 10 to 15 per cent of the total number of cases occur in the first ten years of life, the majority being in the latter half of the decade.

ETIOLOGY.—Diabetes insipidus has no constant pathological anatomy. The cases which have come to necropsy have shown various pathological conditions, mainly involving the brain. The most common anatomical lesion has been tumor, either of neoplastic or inflammatory origin. The most frequent situation for these tumors

has been in or near the floor of the fourth ventricle, or in the hypophysis. On the other hand, tumors in these situations often do not cause the symptom-complex characteristic of diabetes insipidus.

Syphilis is frequently mentioned in the literature as an etiological factor in connection with the lesions found in diabetes insipidus. In such cases the lesion is either a gumma in the floor of the fourth ventricle or hypophysis, a syphilitic basilar meningitis, or a syphilitic endarteritis.

A certain number of cases have been reported in which no demonstrable anatomical lesion was found. The facts have led to the classification of diabetes insipidus under two types: (1) primary or idiopathic, and (2) secondary or symptomatic.

The real etiology and pathogenesis of diabetes insipidus remains unknown. There are three theories in vogue at the present time: (1) that the symptom-complex is due to a faulty power of concentration on the part of the kidney; (2) that it is due to a primary polydipsia of neurogenous origin, with normal kidney function; (3) that it is due to a symptomatic polyuria caused by stimulation of the kidney from a variety of sources, including stimulation through the nervous system, and from hypersecretion of the hypophysis. In my opinion the first theory is improbable, and the weight of evidence is about equally balanced between the last two.

SYMPTOMS.—The symptoms are directed especially to the urine, which is passed in very large quantities; in one case of Trousseau's, in an adult, amounting to twenty-eight quarts a day. There is a very low specific gravity, varying from 1001 to 1005 or 1007. Glucose is never present, but inosite (muscle sugar) has at times been noted. Albumin and casts are of only rare occurrence. The total solids are normal or in many cases greatly increased.

Intense thirst, a dry skin, disturbance in the surface circulation, and general nervous symptoms are often present. Emaciation is not so marked as in diabetes mellitus, but usually takes place gradually. The children are often stunted in growth, the development of bone and muscle being particularly deficient. The appetite is usually good. Often the general health is not interfered with, and the disease may last for a period of years.

DIAGNOSIS.—This condition is to be distinguished from nervous or hysterical polyuria, which is of temporary duration and is associated with other hysterical symptoms.

It is differentiated from diabetes mellitus by the absence in the urine of dextrose or grape sugar, and by the low specific gravity of the urine.

Chronic nephritis may be excluded from the diagnosis by the absence of albumin and casts and the normal total of solids elim-

inated, together with the absence of clinical symptoms of chronic nephritis, and of an abnormal response to tests for renal function.

PROGNOSIS.—The prognosis and course of diabetes insipidus cannot be predicted with any certainty. In the symptomatic cases, the prognosis is that of the disease of the brain which is responsible for the symptoms. Spontaneous recovery has been reported in a few cases, but there is doubt as to whether these were true cases of diabetes insipidus, or only some temporary form of symptomatic polyuria. In the idiopathic cases, the usual course is either gradual exhaustion with a fatal termination, or else death occurs from some intercurrent infection. Some cases, however, may run a chronic course of many years without much affection of the general health, and well-defined polyuria and polydipsia have continued through life, regarded as an inconvenience rather than as a disease.

TREATMENT.—The treatment of diabetes insipidus is very unsatisfactory. A certain number of cases of syphilitic origin have been reported as improving under anti-syphilitic treatment, and this should be tried in all cases in which there is the remotest suspicion of syphilis. Fully as many cases have shown no improvement under anti-syphilitic treatment.

A gradual restriction of fluid intake has been advocated by some writers. Although favorable cases have been reported under this treatment, the benefit is too doubtful, and the discomfort of the patient under restriction of fluid too great, to warrant its general use.

A few cases have been reported of apparent recovery under treatment with hypophysis extract. Herrick has reported a case in which the symptoms appeared to be strikingly relieved by lumbar puncture. There is no conclusive evidence in favor of these forms of treatment, and they have been tried in other cases without apparent result. There is, however, no contraindication for trying them in a chronic case in which the general health is growing progressively worse.

There is considerable evidence that the symptoms can be influenced by changes in the diet. No particular form of feeding has appeared preeminently successful, but the most rational is to use a bland and sufficiently nourishing diet which will not excite excessive polyuria. Such a diet should contain a relatively small amount of sodium chloride, and of nitrogen.

A great variety of drugs have been tried in diabetes insipidus, but no one of them has given any evidence of favorable action.

PROBLEMS AND RESEARCH.—The principal problems awaiting research in connection with diabetes insipidus have to do with the pathogenesis of the symptom-complex. Even if we assume that the unknown cause of the idiopathic cases probably lies in the brain

or hypophysis, as in the symptomatic cases, the most important thing is to determine whether the polydipsia or the polyuria is the primary condition. In favor of the theory of a disturbed function of the kidney being the primary factor, is the experimental production of polyuria by injury to the nervous system, and various studies on the diuretic action of hypophysis extract. A number of studies on the action of the kidneys in diabetes insipidus have been made, with varying interpretations. The weight of evidence appears to point against the theory of loss of concentrative power of the kidneys, and in favor of the fact that the polyuria is produced by pathological conditions of renal stimulation. The principal argument in favor of the theory that the disease is a primary polydipsia, with a resultant polyuria, is that if the kidneys were primarily at fault, the specific gravity would not increase when the fluid intake was restricted, whereas many observations have recorded such an increase of concentration.

R. Fitz has recently reported a case studied by means of the modern methods of testing renal function. In this case the tests showed that the kidneys were apparently normal but gave findings suggesting a vascular hyposthenuria in which the glomerular vessels appeared to be oversensitive to the stimulation of sodium chloride, while other diuretics were inert. These results support the theory of primary polyuria from some pathological stimulus.

Goodall has recently reported metabolism experiments on a case of diabetes insipidus. He believes that the polydipsia is probably primary, as with restricted fluid intake the kidneys secreted a more concentrated urine. His results suggested that the increased katabolism of the body was the result of under-nourishment rather than of the ingestion of large amounts of fluid.

SPASMOPHILIA

(Tetany.)

Spasmophilia is a condition peculiar to the early years of childhood, characterized by hyperirritability of the peripheral nerves to mechanical and electrical stimulation, and by a tendency toward tonic and clonic spasm.

The disease is very common in infancy, and is responsible for much of the tendency toward convulsions which is characteristic of early life.

ETIOLOGY.—Researches on the nervous system have not disclosed any tissue changes characteristic of spasmophilia. There is, however, little doubt that the hyperirritability of the peripheral nerves is due to a *disturbance of metabolism*. No evidence of any

toxin caused by disturbed metabolism has been found. Considerable evidence has been found, however, that the condition is caused or accompanied by an *anomaly of the metabolism of the mineral salts*. It has been shown that the brain of spasmophilic children is poorer in calcium content than that of normal children (Quest), and metabolism experiments have shown that there is a negative calcium balance in spasmophilia. Other investigators have found abnormalities of the metabolism of the alkaline salts, potassium in particular. It is not yet definitely established whether these changes in the mineral metabolism are the actual cause of the nervous hyperirritability, or whether, as in rachitis, they are simply accompanying manifestations of a disturbance of unknown nature which causes both the symptoms and the negative salt balance. The fact that in both rickets and spasmophilia a disturbance of salt metabolism exists, is strongly suggestive of an etiological similarity in the two diseases, which suggestion is strengthened by certain other peculiarities in their occurrence, such as the rarity of spasmophilia in countries where rickets is rare (Japan).

Whether the nervous hyperirritability is caused by disturbance of salt metabolism, or whether both are caused by a metabolic disturbance of unknown nature, the ultimate cause or causes which produce disturbance are not definitely known. We do, however, know a number of facts as to the occurrence of the disease, which are strongly suggestive of an etiological rôle.

In the first place there is evidence that the factor of *heredity* often plays an important part. The tendency toward laryngeal spasm and convulsions often runs in families. Furthermore, spasmophilia is frequently observed in infants with a *neuropathic family history*. The frequency of occurrence of spasmophilia varies with *the time of year*, cases being more common in the winter and spring, as is the case with rickets, especially in March, April, and May. This suggests the influence of lack of fresh air, and bad hygienic surroundings. The age of the child also plays a part; while the disease has been observed in rare cases even in the newborn, it is uncommon before the fourth month, and the most frequent period of occurrence is that *between six and eighteen months*. There can be little doubt that *disturbances of digestion and assimilation* often form the immediately exciting cause for the appearance of spasmophilic symptoms, and the evidence in favor of this connection is so great, that spasmophilia was formerly supposed to be exclusively due to such disturbance, either a reflex phenomenon, or a manifestation of autointoxication ("gastric tetany"). There is evidence that *acute infectious diseases* can increase the severity of spasmophilic symptoms, or cause the appearance of symptoms in latent or cured cases. Finally, *the diet* undoubtedly plays an important rôle in the etiology of the disease.

Spasmophilia is almost never seen in breast-fed infants. Moreover, when spasmophilic infants previously fed on cow's milk are put on human milk, there is usually a rapid disappearance of the symptoms. Finkelstein believes, as a result of feeding experiments, that it is the whey of cow's milk which is responsible for the disorder, and other investigators have reached the same conclusion. The evidence here is very contradictory, another group of investigators concluding that there is no direct connection between spasmophilia and cow's milk (von Pirquet, Thiemich). Under the last hypothesis, the frequent occurrence of spasmophilia in artificially-fed infants is explained by the frequency of disturbances of digestion and metabolism in infants fed on cow's milk, the spasmophilia being secondary to such disturbance rather than due to any specific element of cow's milk.

Finally must be mentioned the recent work on the influence of the *parathyroids* on calcium metabolism, and the experimental production of spasmophilia in animals. This has led to the parathyroid theory of Escherich, which attributes the entire symptom-complex of the disease to anatomical lesions or functional disturbance of the parathyroids.

It thus appears that spasmophilia is probably a disease of complex etiology. The disturbance of metabolism, whether it produces the symptoms *through* an anomaly of salt metabolism, or whether it produces *both* the symptoms *and* the disturbance of salt metabolism, is probably due to numerous etiological factors, such as faulty diet, digestive disturbance, poor hygienic surroundings, lack of fresh air, infections, and so forth. Whether these causes produce disturbances of metabolism directly, or whether they produce it through disturbance of the parathyroids, or in both ways, is yet to be determined.

SYMPTOMS.—Symptomatically, cases of spasmophilia may be divided into four principal clinical types, as follows:

1. Cases in which laryngeal spasm is the principal manifestation.
2. Cases in which eclamptic attacks form the principal manifestation.
3. Cases in which the carpopedal spasm described as *tetany* is the principal manifestation.
4. Cases of a latent character, which do not attract attention and are recognized only by examination.

In all types the principal diagnostic signs characteristic of hyper-irritability of the peripheral nerves are found. The clinical types cannot be regarded as different stages, or different degrees of severity. Many children show only the manifestations characteristic of one clinical type. Other children show a combination of laryngeal spasm with either convulsions, or tetany. We do not know why spasm-

philia is manifested in one child by one clinical type, in another child by another.

The disease shows few general symptoms, and usually the first thing to attract attention is either a convulsion, or a tonic spasm of the extremities, more frequently the former. Laryngeal spasm, although the commonest manifestation of spasmophilia, is rarely recognized as abnormal by the parents unless severe, and is usually recognized only by the physician when the infant comes under his care for some other ailment. In very pronounced cases, the patients are often restless, irritable, fussy, easily frightened, cry a great deal, and allow only certain persons to care for them.

LARYNGEAL SPASM.—The milder forms of laryngeal spasm are the most common manifestation of spasmophilia. The only noticeable symptom is *attacks of crowing inspiration*. The sound of the inspiration much resembles that of common croup, or the whoop of pertussis. The attacks usually come on when the child is disturbed in some way, particularly when it cries or laughs; often every disturbance produces an attack. To the trained ear the inspiratory stridor of spasmophilia is very characteristic, but is usually unnoticed by parents, or by persons not familiar with its significance. Whenever in a crying infant each inspiration is audible as a distinct crowing sound, the physician should suspect spasmophilia and should seek the characteristic diagnostic signs of the disease. It is important to recognize these mild attacks, and to establish the diagnosis, because they sometimes pass over suddenly into the more dangerous, severe form.

The severe form of laryngeal spasm caused by spasmophilia is that often described under the name *laryngospasmus*, or *laryngismus stridulus*. These attacks consist in a sudden complete arrest of respiration through spasm of the larynx. The child's head drops back, and he makes violent efforts to draw air into the lungs, but without result. His eyes start forward, his lips turn blue, his skin becomes covered with a cold sweat, and takes on a bluish-gray color. His consciousness leaves him, his limbs become relaxed, urine and feces are passed involuntarily, and in a few minutes he takes on the appearance of death, except for slight twitching of the eyes and corners of the mouth. Suddenly the spasm relaxes, and a prolonged crowing stridor accompanies the drawing in of air between the closed vocal cords. Deeper inspiratory efforts follow, the stridor diminishing with each, and in a few minutes normal respiration is reestablished, and the child appears somewhat exhausted, but otherwise as well as ever. This is the usual course of the attack, which may be repeated at varying intervals. Sometimes, however, the end is not so favorable, as an attack of laryngospasmus may be fatal. In such

cases, death occurs not from suffocation, but from a stopping of the heart, and consequently artificial respiration is of no avail. One attack may precipitate another, and twenty or more seizures have been observed in twenty-four hours, some severe, some of the mild type. The attacks are much commoner by day than by night, are usually precipitated by some psychic excitation, and do not often come on during sleep, except at the moment of sudden waking. Sometimes an attack of laryngospasmus may be followed by general convulsions. Occasionally the spasm occurs after inspiration when the lungs are filled; this is a dangerous form, and its character is often overlooked because there is no crowing inspiration at the end of the seizure.

Laryngeal spasm is the spasmophilic manifestation which is particularly associated with rachitic children; it is a rare manifestation after the second year.

CONVULSIONS.—The eclamptic attacks of spasmophilia consist in localized or general clonic twitching of the muscles with loss of consciousness. They in every way resemble attacks of true epilepsy. In the milder cases the twitching is confined to the muscles of the cheeks, eyelids, eyeballs, and often the neck. More commonly the entire face and all the extremities are involved, and the convulsion may occasionally be bilateral at the start. Consciousness is lost from the beginning of the attack, the pupils do not react, and the cutaneous reflexes are absent. Only exceptionally is there a stage of tonic spasm. In severe cases the picture is very characteristic, with violent twitching of the face, staring, wide-open eyes, either twitching or turned upward, froth at the mouth, and the entire body shaken by rhythmic jerks. The fontanelle in an attack is tense, the pulse is rapid and irregular, and urine and stool may be passed involuntarily.

The duration of an attack is usually from one-half to two minutes; only very rarely does it last longer than three minutes. One attack may, however, be closely followed by another, causing a "status eclampticus." At the end of the attack the motor irritability usually gradually diminishes, and the child sinks into a sleep, from which he awakes apparently normal. An attack may be followed by a brief febrile reaction, and fever is usually seen when the seizures are frequent. Apart from these attacks, fever is not seen in spasmophilia.

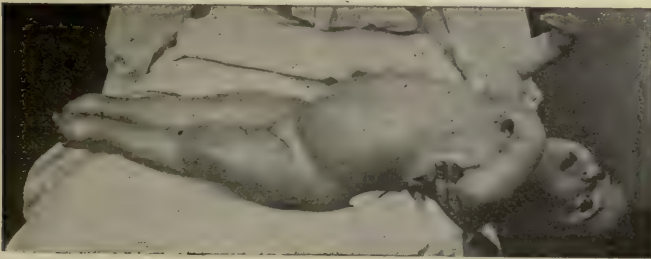
The convulsions of spasmophilia may appear only once, but this is uncommon. Usually the attacks are repeated, but the intervals show the greatest extremes of irregularity. The seizures may occur daily, twice a day, twenty times a day, or at intervals of weeks or months. There is absolutely no rule as to the time and frequency

of the recurrences. Attacks may continue daily for one or two weeks, and then cease abruptly without treatment; they may cease spontaneously at any time. Relatively, these eclamptic seizures are much less dangerous than the severe form of laryngeal spasm.

The attacks often show evidence of being precipitated by some special cause, such as acute digestive disturbance, abdominal distention, or the onset of an acute infection. It is probable that many of the convulsions of early life which are considered to be simply reflex, such as those associated with teething, worms, constipation, and foreign bodies, would show a background of spasmophilia if the cases were thoroughly examined. Many cases originally called epilepsy, which later recover, are probably also spasmophilia.

TETANY.—This type is characterized by a peculiar tonic spasm of the hands and feet. The hands tend to assume the so-called “obstetrical position.” The wrist is sharply flexed and turned out-

FIG. 128



Showing the characteristic spasm of tetany in an infant of 6 months, who was breast fed and showed only slight degrees of malnutrition and rachitis

ward; the thumb in the position of extension is drawn across the palm of the hand beneath the fingers, which are flexed at the metacarpo-phalangeal joints, but otherwise are in the position of extension. The feet are rigidly extended and may be in the position of talipes equinus or of equino-varus. The phalanges of the toes are flexed and extended in the same way as those of the fingers.

These tonic contractions are paroxysmal, and vary greatly in their duration. They usually last about an hour, but may have a duration of only a few minutes, or may last for hours or even days. The contractions are painful at times, especially if efforts be made to overcome the spasm. In prolonged spasm, edema of the hands or feet may appear. The position of the hands is often not typical in very young infants, the phalanges not being so rigidly extended, but the abnormal character of the position can usually be easily recognized. Tetany of the feet is unmistakable.

Other groups of muscles may be involved in tonic spasm in some cases, especially the muscles of the face, causing a peculiar expres-

sion; in severe cases the lips are pushed forward. Occasionally there is a spastic strabismus. The spasm sometimes involves the muscles of the neck, causing a stiffness of the neck and retraction of the head suggesting meningitis. Tonic contraction of the muscles of the back or extremities is seen at times. In rare cases even the musculature of the bladder may be involved, with retention of urine. Occasionally persistent cases of tetany are seen, in which the tonic spasm of the limbs persists for days or weeks; these persistent forms are seen most often in infants emaciated from gastro-intestinal disease.

LATENT CASES.—A certain number of babies do not show any of the three foregoing types of spasmophilia, namely, laryngeal spasm, convulsions, and tetany, but nevertheless show the signs of the disease on physical examination. Such cases may be considered as showing a latent type of spasmophilia.

PHYSICAL SIGNS.—All the clinical types described above are recognized as belonging to the general symptom-complex of spasmophilia, because they show certain signs on physical examination which are characteristic, and diagnostic of the disease. There are three signs characteristic of spasmophilia, and the presence of any one of them is sufficient to establish the diagnosis. They are, (1) increased irritability to galvanic stimulation; (2) Chvostek's sign; (3) Trousseau's sign.

GALVANIC HYPERIRRITABILITY. (*Erb's Phenomenon.*)—This was described by Escherich, and studied by Mann and Thiemich. It depends upon the fact that in the normal child, when the Stintzing electrode is applied over the peroneal nerve, no cathodal or anodal opening contraction is produced with less than five milliamperes of galvanic current. In the hyperexcitability characteristic of spasmophilia, cathodal and anodal opening contractions are produced by much weaker current, down to one milliampere. For ordinary clinical testing of the electrical reactions, *the presence of a cathodal opening contraction with less than five milliamperes of galvanic current, may be considered to establish the diagnosis of spasmophilia*, while the absence of such a contraction excludes it.

The testing of the electrical reactions is a difficult procedure, requiring special training, and cannot be generally used for diagnostic purposes. In very young children, or during convulsions, or with very marked tetanic contraction, a satisfactory test is sometimes impossible. The indifferent electrode is applied to the breast, while the differentiating electrode is applied to the part of the nerve nearest the surface. The median nerve at the bend of the elbow may be used, or the peroneal nerve, or the ulnar nerve. Voluntary movements are easily to be distinguished from the contractions caused by the galvanic current.

CHVOSTEK'S SIGN.—While the testing of the electrical reactions is the most thorough method of investigation in suspected spasmophilia, the testing for mechanical hyperirritability is simpler, and more easily carried out in ordinary clinical examination. This consists in percussion over the nerve trunk, which causes a rapid contraction just as if the nerve were electrically stimulated. The test is easiest to carry out on the facial nerve. The physician strikes a series of sharp taps with the tip of the finger on various parts of the outer part of the cheek. When he strikes a nerve trunk there will be a rapid contraction of the muscles supplied by the nerve. This is called *Chvostek's sign*. Sometimes all the muscles supplied by the facial nerve are involved in the contraction, but more often either the lower branches are struck, producing a contraction of the muscles about the mouth, or the upper branches, producing a contraction of the muscles about the eye (Weiss' phenomenon).

It must be remembered that Chvostek's sign is not by any means as constant in spasmophilia as is the increased galvanic excitability. Its chief value is in infancy; it is usually present in spasmophilic infants, and when present is diagnostic. It can, however, be absent even in the spasmophilia of infancy, and is more likely to be absent in older children. Sometimes when the facial phenomenon is absent, contraction in the hand or foot may be obtained by tapping over the appropriate points of the radial or peroneal nerves. This should be tried in such cases, particularly if the physician is not prepared to test the electrical reactions.

The presence of Chvostek's sign is sufficient to establish the diagnosis. The absence of the sign, however, does not exclude spasmophilia.

TROUSSEAU'S SIGN.—This depends on the fact that in spasmophilia, compression of the nerve trunks of the upper arm will cause the hand to assume the contraction characteristic of tetany. An elastic constriction band is put about the arm in the region of the bicipital fork, and is left in place for several minutes. In positive cases, the hand assumes the characteristic "obstetrical position," from which it can only be moved by the use of force.

When present, Trousseau's phenomenon is diagnostic; it is, however, often absent in spasmophilia. An objection to its general use is that it is somewhat painful. Furthermore, in children showing the type of spasmophilia characterized by laryngeal spasm, the testing of Trousseau's phenomenon may precipitate an attack, with its attendant dangers. This sign should only be tested if apparatus for testing the electrical reactions is not at hand, and if both Chvostek's sign and the peroneal reflex are absent.

COURSE AND COMPLICATIONS.—Spasmophilia tends to run

rather a long course, but the progress of a case is very irregular. When untreated, it usually tends to persist for months, but at any time, without any particular treatment, there may be a sudden improvement, or even a disappearance, of all symptoms and signs, including the electric hyperirritability. This irregularity in the course of the disease makes it very difficult to draw any positive conclusions as to the result of any particular method of treatment. When the instituting of treatment is followed by prompt disappearance of symptoms, and the electric reactions become normal, one is tempted to conclude that the treatment brought about the improvement. It may be so, but one should remember that similar improvement may occur suddenly without treatment.

Even when, with or without treatment, improvement occurs, it does not necessarily mean that the disease is cured. The manifest symptoms of the disease—laryngeal spasm, convulsions, or tetany—usually improve rapidly under treatment. The increased electrical excitability may be more obstinate. This too, however, may disappear with or without treatment. Later, with a change of diet, change of surroundings, or without obvious cause, the symptoms are very apt to recur. In cases treated by feeding with human milk, the symptoms are particularly apt to recur when cow's milk is given again. Patients may be free from signs of spasmophilia in summer, with recurrence in winter. The course of every case is different. The symptoms may be confined to one clinical type, or may pass over into another.

One complication, or rather manifestation, of the disease remains to be mentioned. In all forms of spasmophilia, sudden death occasionally occurs. The cause is sudden cessation of the heart, and this may occur not only during an attack of laryngeal spasm, or less often during a convulsion, but occasionally without any paroxysmal manifestation. A large meal appears to be the usual precipitating cause in such cases. These sudden deaths in spasmophilia have been particularly described by European writers, but I have seen them in this country. The cause of death is supposedly a tetany of the heart-muscle. It is probable that many deaths attributed to "status lymphaticus" for lack of other discoverable cause, were really cases of spasmophilia.

DIAGNOSIS.—The diagnosis depends on the finding of electrical or mechanical overexcitability of the peripheral nerves. Chvostek's sign, or Trousseau's sign or a peroneal reflex or increased electrical reactions, when positive, are diagnostic.

In a well-marked case of the tetany type, or in a case with typical severe laryngospasmus, the diagnosis is unmistakable. The common mild type of laryngeal spasm is, however, not necessarily of spas-

mophilic origin, as the same symptom is sometimes seen in other diseased conditions. In an infant, however, it should always suggest spasmophilia, unless some other obvious cause be present. The diagnosis is confirmed by the finding of the characteristic physical signs of the disease.

The type characterized by convulsions must be differentiated from the various other conditions in which convulsions are seen. Those principally to be considered are epilepsy, convulsions of reflex or toxic origin, and convulsions symptomatic of organic disease of the brain. The spasmophilic origin of the convulsions is recognized by the signs of electrical and mechanical hyperirritability of the nerves. If the presence of the characteristic signs shows the child to be spasmophilic, it makes little difference whether or not the immediately exciting cause be reflex or toxic. It must be remembered, however, that the spasmophilic child may have meningitis, encephalitis, or other organic disease of the brain, and the presence of spasmophilia should not lead to the overlooking of the signs of these other diseases. Epilepsy is distinguished from spasmophilia by absence of Chvostek's sign, and normal electrical reactions.

PROGNOSIS.—The majority of cases of spasmophilia eventually recover. The only immediate danger is the sudden death which occurs in a few cases. A study of the later history of spasmophilic children has shown, however, that quite a number of them show some signs of neuropathy or of defective intelligence, and in only about a third is development wholly normal. There is no evidence that spasmophilia ever passes over into epilepsy.

TREATMENT. PROPHYLACTIC.—The important factors in the prophylaxis of spasmophilia are *maternal nursing, sunlight, and fresh air*. If a baby is breast-fed, with good hygienic surroundings and plenty of fresh air, spasmophilia will not develop.

HYGIENIC.—Hygienic treatment is fully as important in spasmophilia as in rickets. The ideal treatment is the same as that described for rickets, the essentials being fresh air, sunlight, and exercise. All the hygienic measures described for rickets should be employed in cases of spasmophilia.

DIETETIC.—The most valuable of all known curative agents in spasmophilia is *human milk*. Whether or not it can be employed in an individual case depends upon various circumstances, such as the ease with which a wet-nurse can be obtained, and the severity of the spasmophilic manifestations. It must be remembered, however, that the most certain and effective cure for spasmophilia is human milk.

When in spasmophilia it is necessary to use artificial feeding, the basis which can serve as a guide in the modification of cow's milk

is somewhat uncertain, because it has never been finally proven whether some particular element of cow's milk is responsible for the symptoms, or whether they are caused by the general difficulty of digestion with cow's milk. With our present knowledge it is best not to use a whey-mixture, and to substitute as far as possible some other form of carbohydrate, such as dextri-maltose, for lactose. It is also advisable to begin to add starch to milk-mixtures as early as the digestive powers of the child will permit. The whey salts may be further reduced by using precipitated casein. Some such formula as fat 3%, dextri-maltose 6%, protein 1.5%, starch .75%, may be chosen to begin with, and if precipitated casein can be made or obtained, the protein may be given in that form. Further modification must be guided by the digestive peculiarities of the individual child, according to the general principles of infant feeding. It is important to eliminate all forms of indigestion.

With older infants, able to take a more varied diet, cow's milk can be excluded, or reduced to a minimum. Bread, cereals, butter, beef juice, meat, and vegetables can take the place of milk at this age. Overeating should be avoided, and the child should never be allowed to eat a very large meal.

When the symptoms of spasmophilia have disappeared, cow's milk should be added gradually to the diet. It is often necessary to exclude cow's milk for weeks or months, if a recurrence of symptoms is to be prevented.

MEDICINAL.—Three methods of specific medicinal treatment have been recommended in spasmophilia, as follows: (1) The giving of calcium salts; (2) the giving of phosphorus and cod liver oil; (3) the giving of parathyroid extract.

Calcium was first given in the form of calcium lactate. Some observers claimed good results, others failed to get them. The original dose was 3 to 5 grains three times a day. Later larger doses were recommended. At the present day *calcium chloride* is preferred to calcium lactate. Several observers have reported good results as measured by the electrical reactions, from the giving of calcium chloride, if the drug is given in sufficiently large doses. Bluhdorn gives from 2 or 3 to 4 or 8 grammes daily. Sedgwick, in this country, has published very good results from calcium chloride given in doses of at least 3 grammes (75 grains) daily. The salt is given in divided doses in the feedings, and infants do not seem to object to the taste. The question of the value of calcium therapy must be regarded as still *sub judice*. Most observers believe that the effect is only to diminish the symptoms, and that it is only temporary. It is difficult to conclude as to the value of any therapeutic procedure in a disease of indeterminate course like spasmophilia. It is certain

that in effectiveness calcium chloride cannot be compared with human milk. I believe, however, that it may be tried in severe or obstinate cases for which human milk cannot be obtained, or in which human-milk fails to effect a cure. My results have failed to give the slightest evidence of any specific value of calcium chloride.

The combination of phosphorus with cod liver oil has been widely advocated in Germany as a method of treating spasmophilia as well as rickets. The basis for its use is certain metabolism experiments which show that the combination favors the retention of calcium. There is, of course, no positive proof of its clinical value in spasmophilia. Its advocates believe that its good effect is more permanent than that of the calcium salts. Rohmer has recently published a paper in which he claims the best results from a combination of calcium therapy and phosphorlebertran. The combination of phosphorus and cod liver oil may be given in the same doses as described under rachitis.

Parathyroid extract has been recommended in spasmophilia, on account of recent research on the rôle of the parathyroids in the etiology of the disease. There is at present little evidence that it has any value.

SYMPTOMATIC.—The clinical manifestations of spasmophilia may be aided by various temporary measures. At the beginning of an attack, whether the manifestation be laryngeal spasm, a convulsion, or an attack of tetany, a dose of two teaspoonfuls of castor oil should be given, and feeding with cow's milk should be stopped at once. If the abdomen be distended, a high irrigation of the colon should be given, and this may be repeated if necessary. For twenty-four hours, only boiled water or barley water should be given, and then feeding with human milk should be begun, and continued as long as possible. If human milk be unobtainable, the cow's milk modification given after twenty-four hours should be weak at first.

When the patient is seen in a convulsion, a warm bath should be given, followed by castor oil and irrigation of the colon. If the convulsions continue or are frequently repeated, sodium bromide, 5 to 15 grains with chloral hydrate 1 to 5 grains in 1 ounce of water should be given by rectum, and repeated if necessary every two hours for three or four doses. An infant of one month can be safely given by rectum 1 grain of chloral; of six months, 2 grains; of twelve months or over, 5 grains. If this is not effective, or while waiting for it to take effect, the inhalation of ether in small amounts may be used for severe convulsions. At times, a tendency to repeated convulsions can be checked by lumbar puncture.

The milder attacks of laryngeal spasm require no symptomatic treatment. It is important, however, to prevent all possible causes

of sudden psychic disturbance. Sudden noises or disturbance, inspection of the throat, unnecessary physical examination, the entrance of strangers into the room—all these should be avoided. If there has ever been an attack of severe laryngospasm, the child should be watched day and night, and a basin of cold water, together with a hypodermic syringe filled with camphor in oil should stand ready beside the bed. When a severe attack occurs, if the child does not quickly breathe, it should be sprinkled with cold water. If apnea continues, the finger should be pressed under the tongue, and if this is not followed by an inspiration, an injection of camphor in oil should be given, followed by efforts at resuscitation by artificial respiration. The moment the crowing inspiration occurs, all therapeutic endeavors should cease, in order not to precipitate a second attack.

When the only manifestation of spasmophilia is carpopedal spasm, symptomatic treatment is not usually indicated, reliance being placed on the effect of the general hygienic, dietetic, and medicinal treatment. When the tonic spasms are particularly severe, sodium bromide may be given in doses of 5 grains every four hours.

PROBLEMS AND RESEARCH.—An enormous amount of research work has been devoted to the subject of spasmophilia in the last decade. The principal problems confronting the investigator have been indicated in the discussion of the etiology of the disease.

The first feature of spasmophilia to attract the attention of investigators was the apparent relation to the diet. Feeding experiments with the various elements of cow's milk gave no positive evidence in support of Finkelstein's theory of a whey injury. Since there is five times as much calcium in cow's milk as in human milk, the theory was advanced that spasmophilia represented a calcium intoxication. Stoelzner explained this by assuming that the excessive calcium in cow's milk is absorbed, but must be re-excreted by the intestinal mucosa. On account of the extraordinary demands thus made upon the excretory functions, they become insufficient, with a resulting calcium retention and intoxication. While certain experiments in feeding with excessive calcium have apparently given positive results in support of this theory, it has been attacked by many writers, and the weight of evidence is decidedly against it, most experiments proving that there is no increased calcium retention in spasmophilia.

Certain researches tending to prove that the action of calcium on nerve tissue was depressant, and that its withdrawal was excitant, led to the experiments of Quest, who found a diminished calcium content in the brains of spasmophilic infants. These results turned the attention of investigators to the theory that the symptoms in spasmophilia are due to calcium deficiency. The results of a great

mass of research work in connection with this theory may be summarized as follows: (1) There is in spasmophilia evidence of a negative calcium balance; (2) there is evidence of a disturbance of the metabolism of the mineral salts in general; (3) there is evidence that the metabolism of the mineral salts has an influence on the functioning of the nervous system, some salts acting as excitants, others as depressants.

If these conclusions be accepted, we are next confronted by three further problems:

1. Are the symptoms produced directly by the disturbance of salt metabolism, or is this only a coordinate manifestation, the symptoms being produced by other substances, possibly of a toxic character?

2. If the symptoms are produced by a disturbance of salt metabolism, how can the relation of spasmophilia to the diet be explained?

3. If the symptoms are produced by a disturbance of either the salt metabolism, or the intermediary tissue metabolism, what is the ultimate cause of the disturbance?

In the investigation of the first question, no evidence has been found of any toxic substances causing nervous hyperirritability. There is considerable evidence that the symptoms are produced by an actual disturbance of the mineral metabolism. For example, in a recent research, MacCallum, Lambert and Vogel found that when calcium was removed from blood by dialysis, and the blood perfused through an isolated extremity, extreme hyperexcitability of the nerves was produced. There is some evidence that it is the relative proportions of calcium and other salts which is concerned in producing the symptoms, rather than the actual calcium content.

In connection with the second question, the fact remains that spasmophilia is usually seen in artificially-fed infants, and that human milk is its most effective curative agent. This is strongly suggestive of some special exciting substance in cow's milk, and this does not fit well with the theory that a disturbance of salt metabolism is the cause of the disease. There are still many authorities who believe that the whey of cow's milk has a particular rôle as an etiological factor. Pediatricians are especially prone to attribute pathological processes to diet. The weight of evidence certainly suggests that cow's milk is not the only factor in spasmophilia. If it has no specific rôle, the relation of spasmophilia to artificial feeding can only be explained on the ground that disturbances of metabolism in general are more common in artificially-fed infants.

The third problem, that of the ultimate cause of the disturbance of metabolism, is the one which is stimulating the greatest activity in research at the present day. It is obviously closely connected

with the question of the rôle of diet. There are two principal theories for the cause of the disturbance of metabolism. These are the following:

1. That the disturbance is due to a variety of causes, among which are unsuitable food, indigestion, lack of fresh air, faulty hygienic surroundings, acute infections, and so forth.
2. That the disturbance is due to anatomical or functional insufficiency of the parathyroid glands.

These two theories are not mutually exclusive. It is very probable that the various causes enumerated in the first theory may all play an etiological rôle. The question is whether the influence of the parathyroids is a necessary feature in the production of the disease. The literature of the last few years is full of investigations upon this point

The parathyroid theory of tetany and spasmophilia depends on the fact that tetany may be produced experimentally in dogs by extirpation of the parathyroids. A great number of writers have attempted to show that this experimental tetany is identical with postoperative and spontaneous human tetany. The chief argument in favor of this is the identity of the clinical symptoms, and of the disturbance of calcium metabolism.

The theory has been attacked by a number of writers, chiefly those who believe strongly in the dietetic origin of spasmophilia. The arguments against the parathyroid theory are that it is a mere hypothesis, unsupported by any pathological or anatomical findings. Also, since milk diet seems to be favorable in the experimental tetany of dogs, it has been argued that spasmophilia and experimental tetany are entirely different conditions. The reply to this has been that pediatricians are too anxious to find things to prove the dependency of tetany on diet.

A number of statistical post-mortem researches have been published on the parathyroids. Erdheim first described hemorrhages into the parathyroids, occurring at birth, and a number of investigators have found hemorrhage, or the residuals of hemorrhage, in the parathyroids in numerous post-mortems of infants. On this ground, a number of authorities believe that spasmophilia is caused by disturbed or lowered parathyroid function, due to the effect of these hemorrhages.

Other investigators have failed to find very much evidence of an anatomical lesion of the parathyroids. Still others have found such traces, without evidence of spasmophilia.

Among recent investigators are a number supporting the hypothesis that spasmophilia is caused, not by traumatism of the parathyroids during birth, but rather by subsequent disturbance of their

function. This theory is consistent with the theory that diet, hygienic conditions, and so forth, play an etiological rôle.

There will probably be much research on the metabolism and the chemistry of the blood, both of human and experimental spasmophilia in the next few years

In therapeutics the principal question awaiting final solution is the value of calcium chloride medication. Also, a recent contribution by Berend is based on the theory that there is disturbance both of calcium and magnesium metabolism in spasmophilia, and claims good therapeutic results from the subcutaneous administration of magnesium sulphate. Parathyroid extract will probably be more extensively tried before it is finally condemned.

PELLAGRA

Pellagra is a disease characterized by certain definite pathological changes involving the skin, the nervous system, and the gastrointestinal tract, and other organs. The disease was first described by Gaspar Casal of Spain in 1735. The name pellagra was first used by Frapolli of Italy in 1771, who adopted the term in general use among the Italian peasants, meaning rough skin. Since then the disease has been described under many different names.

The disease is very common in certain localities. It is apparently very much on the increase in the United States. It is only comparatively recently that its occurrence among children has been adequately recognized. It has been known that in Italy pellagra is of comparatively frequent occurrence in children, and even in infants. Recently its occurrence among children has been recognized in this country, but there are few statistical studies showing its frequency. Lavinder found in a study of 15,870 cases of pellagra, 412 under five years of age, and 1,719 between the ages of five and fifteen years. The consensus of opinion among the physicians of the South, so far as can be determined from a number of recent publications, appear to be that the frequency of the disease in childhood is about 10 per cent.

From the time of its first recognition the disease has been associated with the eating of Indian corn. Until recently the prevalent theory of etiology has been that pellagra is due to the eating of spoiled maize. The most recent investigations have brought forward evidence which renders the spoiled maize theory very improbable. I have classified pellagra among the disturbances of nutrition and metabolism, not because I am convinced that the preponderance of evidence is in favor of the dietary theory of etiology, but simply for convenience of reference until the weight of evidence shall, by future research, be brought to incline toward one view or the other.

ETIOLOGY.—The cause of pellagra is unknown. The available evidence bearing on etiology, has given rise to two distinct theories as to the cause of the disease.

1. The first theory is that pellagra is due to an improper diet. The most recent evidence, while against the spoiled maize theory, points toward the association of pellagra with a vegetarian diet, containing a preponderance of cereal. This has been explained on the theory of the vitamins, advanced by Funk. A cereal diet is supposed to be deficient in certain substances essential to proper nutrition and metabolism. This theory would bring pellagra into the same etiological group as beriberi and scurvy. Other suggestions in connection with the dietetic origin of pellagra, are that it may be caused by the toxic action of substances like aluminum, which are present in large amounts in cereals, or to silica, which is present in excess in certain drinking waters. A deficiency of amino acids has also been suggested as a possible explanation of a dietetic etiology.

2. The second theory is that pellagra is an infection, caused by a parasite. The brilliant researches of Sambon constitute the chief foundation for the parasite theory. Sambon believes that the disease is an insect-borne infection caused most probably by a protozoal parasite, and transmitted by a fly of the genus *Simulium*. The *Simulium reptans*, incriminated by Sambon, is not found in this country, but the *Simulium vittatum*, or buffalo gnat, is frequently encountered. Some writers are inclined to suspect this insect, while others believe that in this country the evidence should eliminate the *Simulia*, but believe that the disease is transmitted by some other variety of biting insect.

The evidence for and against these two theories appears to be fairly evenly balanced. It will be further discussed under Problems and Research. There are certain known facts of importance in connection with the etiology of the disease.

AGE—No age is exempt. The disease is comparatively rare in infants under two years of age, and very rare in infants under three or four months. In children, pellagra occurs most often between the ages of two and ten years. It becomes less common again in the first years after puberty.

SEX.—The preponderance of victims among the female sex is a notable characteristic of the disease in adults. In children this does not hold, and the disease appears to be about equally distributed between the sexes.

CLIMATE AND DISTRIBUTION.—Pellagra appears to be very generally distributed, and no climate or country is entirely exempt. There are, however, very marked variations in the frequency of

pellagra in different localities. In the United States, the disease is commonest in the Southern States. Even in the South there are interesting variations in the distribution of the disease, which contribute additional interest to the problem of etiology. In the North the disease has generally been regarded as rare or non-existent. In recent years this has been shown to be untrue, and an increasing number of cases are being reported from Northern communities. Physicians in every part of the United States should be on the watch for cases of pellagra. The disease appears to be notably on the increase in this country.

SEASON.—There is a well-marked seasoned incidence in pellagra. Most of the cases occur in the spring, early summer, or autumn. It is very unusual for cases to appear during cold weather. Recurrent attacks are seen at times, as in malaria, occurring each year at a certain season.

HEAT.—There is no definite evidence that it is the heat of our Southern climate which is responsible for the greater frequency of pellagra in the South. There is some evidence, however, that the rays of the sun aggravate the cutaneous eruption, and that they may act as a contributory cause in the acquirement of the disease.

SURROUNDINGS.—There is a notable relation between the occurrence of pellagra and the surroundings of the patients. It has not been established that pellagra is more common in the rural districts, or among field workers. The disease is found most often under conditions of unsanitary surroundings, whether in rural districts, or in cities. In certain parts of the South it is particularly common in the mill villages.

DIET.—In spite of the fact that the maize theory of pellagra is improbable, nevertheless there is some evidence of a relation to the diet. Pellagra seems to be associated with a vegetarian diet, and many cases have improved when more animal protein was given. The diet of the poorer classes in the South is largely cereal. No more definite relation between pellagra and the diet has been established.

IN FAMILIES.—Sambon states that in pellagra districts he has often found the parents and all of the children attacked. Siler and Garrison report that in one-half of the cases observed, only one case occurred in a family, in a quarter of the cases there were two in a family, and in the remaining quarter there were family groups of three, four, and five. There is, however, no evidence of direct contagion.

PATHOLOGICAL ANATOMY.—The lesions of pellagra in children show no essential differences from those of adults. For a de-

tailed account of the pathological anatomy of pellagra, the reader is referred to the special literature of the subject. The lesion of the skin is an angioneurotic process similar to that of erythema multiforme. In the internal organs the essential lesion is a perivascular infiltration with mononeuclear cells. The most marked internal lesions are found in the nervous system and in the gastro-intestinal tract. In the nervous system various degenerative changes are found, which apparently represent, not a systemic, but a diffuse process, suggesting a toxic degeneration, and affecting both nerve cells and nerve fibres. In the spinal cord these changes are most marked in the columns of Goll and Burdach. The changes in the gastro-intestinal tract appear to be an essential part of the disease rather than secondary manifestations. They consist chiefly of chronic catarrhal inflammation, with exfoliation of epithelial cells, and infiltration of the stroma.

SYMPTOMS.—The principal features of the symptom-complex of pellagra, are *symmetrical skin lesions, gastro-intestinal disturbances, and certain nervous manifestations.*

CUTANEOUS MANIFESTATIONS.—The symmetrical skin lesions of pellagra are considered pathognomonic. The rash varies very much in intensity, which causes corresponding variations in its appearance. The general character of the rash is that of a dermatitis. In the mildest form, the eruption presents the appearance of a pinkish or reddish erythema. In more severe cases, there is a marked reddening of the skin resembling sunburn. In a later stage, the rash may present a grey scaling appearance. After the rash has persisted for some time, there is often marked thickening of the skin, and at times numerous fissures are formed. In some cases there may be a formation of bullae, this being called the wet type, in contradistinction to the dry type characterized only by erythema and scaling or thickening of the skin.

Both the wet and the dry types occur in children. The dry type is, however, very much more common in childhood than the wet type, and was the only form of rash observed by Rice in the orphanages of the South.

The distribution of the rash is peculiar. It is found most commonly on the exposed portions of the body. The commonest site of the rash is the backs of the hands, and the dorsal surface of the feet. In some cases only the hands are affected, and lesions on the backs of the hands were lacking in only 5 per cent of Wood's 189 cases in children. In a certain number of cases the rash, beside appearing on the backs of the hands and feet, extends up the ulnar side of the arms to the elbows, and up the calves of the legs to the knees.

The rash may less commonly invade other portions of the body. The neck and face are affected next in frequency to the extremities. The extent of the invasion is variable. Casal's "necklace," extending completely around the neck, and the "mask," involving the entire face, are rare. Weston has observed the rash in children occasionally on the palms and soles, on the front of the legs, and on the abdomen.

FIG. 129



Annie V., white, aged 6; fifth attack of pellagra; first attack occurred before the age of 2

The duration of the rash is very variable. It may disappear rapidly, leaving the skin somewhat smooth and glistening. Usually, however, it persists for an indefinite period, and finally disappears by desquamation, leaving the skin smooth, and somewhat lighter in color than the adjoining skin. Itching and burning may be present, especially during the stage of desquamation.

The essential feature of the rash of pellagra is its symmetrical character. Although it appears chiefly on the exposed surface, it cannot be prevented from appearing by protection from the sunlight.

THE MOUTH.—The tongue in pellagra usually appears very red, and is often fissured. These appearances are due to a partial loss of epithelium, and to a glossitis. The redness is especially notice-

FIG. 130



Josiah P., aged 18 months; wet variety of pellagra.
(By courtesy of Dr. J. J. Watson, Columbia, S. C.)

able at the sides and tip. The entire mucous membrane of the mouth is sometimes redder than normal, but does not often in children have the fiery redness seen in severe cases in adults. The lips are also often fissured.

GASTRO-INTESTINAL SYMPTOMS.—These are more pronounced, according to Weston, in very young children than in those over four

FIG. 131



Pellagra in Italy. Photograph from Dr. Eugenio Bravetta, Mombello, Italy

years old. Young children show a tendency to indigestion, and often suffer from severe diarrhea. Constipation is seen at times.

NERVOUS SYMPTOMS.—In general, the manifestations of disturbance of the nervous system in children are less common and less marked than in adults. Rice found few nervous manifestations in his series, except in the patellar reflexes which were most often exaggerated, but were sometimes decreased or absent, and only

infrequently normal. Weston states that paresthesia is common in children, insomnia is often marked, and depression occurs in many cases.

BLOOD AND URINE.—The blood changes in pellagra do not appear to be especially characteristic. An increase in the relative number of small lymphocytes has been observed in a number of cases. Indicanuria is very common in pellagra, but is not constant.

DIAGNOSIS.—The only pathognomonic sign on which the diagnosis of pellagra can rest with any certainty, is the characteristic sym-

FIG. 132



Pellagra (By courtesy of Dr. William Weston, Columbia, S. C.)

metrical dermatitis. It is on this that the diagnosis depends in the majority of cases. Prompt recognition of the disease is essential to success in treatment, and the presence of pellagra in all parts of the country, makes it within the range of possibility that a case may be encountered at any time by any physician. Cases of pellagra are likely to be overlooked chiefly because this possibility is likely to be forgotten, and in districts where the disease is uncommon, it may not be recognized only because it is unfamiliar, and has but little meaning to the physicians of that locality. If the possibility of the occurrence of pellagra be remembered, and if the characteristic

cutaneous manifestations be present, the diagnosis of the disease will present but little difficulty.

The question is important whether or not the diagnosis of pellagra in children can be made without the presence of the rash. In a locality in which pellagra is rare or has been unknown, such a diagnosis must always be doubtful; in a region where pellagra is endemic, it will be less hazardous. When in a child are found such symptoms as a red tongue, fissured lips, diarrhea, insomnia, restlessness, paresthesia, exaggerated or absent knee-jerks, or other nervous symptoms not to be explained by any other recognizable disease, the possibility of pellagra should be considered. Often under such circumstances, the

FIG. 133



Pellagra in Italy (By courtesy of Dr. William Weston, Columbia, S. C.)

appearance of an erythema, however slight or transient on the characteristic parts of the skin, will confirm such a tentative diagnosis.

There is no positive laboratory method of making the diagnosis. The changes in the blood, and the indicanuria are not sufficiently marked and constant, to be of much diagnostic value. Whenever the classical triad of symptoms, dermatitis, intestinal disturbance, and nervous disturbance is present, the diagnosis is certain.

PROGNOSIS.—The prognosis is probably very uncertain in young infants. In older children, the disease is milder, and with proper treatment, recovery usually occurs. The period during which re-

lapses are likely to occur is very indeterminate, and consequently cases which have apparently recovered should be kept under observation for a number of years.

TREATMENT.—Hygienic measures are of the first importance in the treatment of pellagra in children. Whenever possible, a complete change of environment should be carried out. The patients should, if it can be arranged, be taken to a locality in which pellagra is unknown. If such a change cannot be managed, the hygienic conditions under which the patients live should be improved as much as possible.

The uncertainty as to the etiology of the disease gives rise to a lack of definite therapeutic indications. The only suggestion comes from the dietary theory of the disease. With our present knowledge, a change of diet is advisable in all cases. Certainly, with infants nursing pellagrous mothers, the infant should be weaned. In artificially-fed infants, the diet should be as liberal as the digestive powers of the child will permit. Cereals should be kept at a minimum, and such articles as beef juice, broths, meats, and eggs, given as soon as possible.

In older children, corn products should be prohibited, and the diet should be so arranged as to contain plenty of animal protein. Foods leaving a large undigested residue should be avoided.

Among other hygienic measures, hydrotherapy has always ranked high in pellagra. The affected areas of the skin should be protected from the direct rays of the sun. Soothing lotions, such as that containing calamine, should be applied to the dermatitis. Internally tonics, such as arsenic and iron, are valuable.

PROBLEMS AND RESEARCH.—At the present time, pellagra presents a most fascinating problem in etiology, in which many methods of investigation are available. It is quite probable that the continued statistical study of the peculiarities of distribution of the disease, such as is being carried out by various commissions, will throw much light on the pathogenesis of the condition. There is also a wide field for experimental study, by means both of dietary methods, and by animal inoculations.

The principal evidence in favor of the nutritional theory is of a negative character, its advocates regarding the burden of proof as resting upon those who believe the disease to be of infectious origin. Lavinder and Francis carried out a very thorough series of inoculation experiments on monkeys, failing to obtain any positive results. Willets and Waring, in their epidemiological studies in the Georgia sanatoria, failed to find evidence of transmissibility, but believed that their results supported the dietary theory, the disease being most prevalent among those whose diet contained little meat and

animal protein. The influence of diet in promoting recovery is believed by many to be sufficiently obvious to constitute evidence as to etiology.

The arguments in favor of the parasitic theory are many. In the first place, the peculiarities of distribution and of seasonal incidence are strongly suggestive of an insect-borne contagion, especially the seasonal recurrences which have been observed. There is no definite evidence in favor of the maize theory or the dietary theory. The recent report of the Illinois Pellagra Commission found no connection with occupation, but evidence of definite spreading from certain centres. There is no evidence, however, incriminating the Simulium.

DIVISION VII

SPECIFIC INFECTIOUS DISEASES

An infectious disease is one caused by a parasitic microorganism. A *specific* infectious disease is one in which the pathological changes in the body are caused by one variety of microorganism only, and are peculiar to infection with that one organism. There are certain microorganisms which produce pathological changes which are in no way specific, sometimes in one part of the body, sometimes in another. The lesions produced are not peculiar to the particular microorganism, but the same tissue changes, and the same disturbances of function, may be produced by other organisms. Examples of such infecting parasites are the common pyogenic organisms, such as the staphylococcus pyogenes, and the streptococcus pyogenes. Other examples are seen in the gonococcus, the bacillus of dysentery, and the colon bacillus. The clinical picture presented by infection with this group of organisms depends not so much upon the nature of the infecting organism, as upon the organ or part of the body which happens to be attacked. For this reason these diseases are described under the various organs or regions of the body which may be involved.

The border line between this group and the *specific* infections, however, is not very sharp, and in certain cases the distinction must be somewhat arbitrary, dependent upon convenience of description. For example, in lobar pneumonia the pathological anatomy of the lung, and the clinical picture produced, are peculiar to infection with the pneumococcus, and from this point of view the disease should be described among the specific infections. The pneumococcus, however, does not produce lobar pneumonia only, but may attack a great variety of organs, producing pathological changes which are in no way specific. Furthermore, the clinical description of lobar pneumonia is much more conveniently placed under the Diseases of the Lungs, where it can be brought into telling contrast with other forms of pneumonia.

Again, it is a question whether the lesions or the symptoms of infection with the bacillus of influenza are sufficiently peculiar to that organism to warrant the classing of influenza as a specific infection. Its chief title to a place in this division is its tendency to epidemic occurrence.

Neither the lesion nor the clinical picture of epidemic cerebrospinal meningitis is in any way characteristic, as practically the same changes in the central nervous system can be produced by the streptococcus, the pneumococcus, the bacillus of influenza, and other organisms. The diplococcus of epidemic meningitis, however, is concerned in the production of no other disease, and the occurrence of this form of meningeal infection in epidemics, together with the fact that it has a specific serum therapy, are the reasons for describing it among the specific infections.

The organisms causing rheumatic fever and erysipelas have not been shown to be specific, but belong in the general streptococcus group. On account of the peculiarities of the lesions and symptomatic manifestations, they are for convenience described in this Division.

There are a certain number of diseases classified among the specific infections, in which the cause has not been discovered. The evidence of an infectious origin for these diseases lies in the fact that they are highly *contagious*, that is, easily transmitted from one individual to another by contact, the same peculiar lesions and symptoms being reproduced after transmission. There can be no doubt that each of these diseases is a specific infection, of which the cause is yet to be discovered. In this group belong scarlet fever, measles, rubella, varicella, variola, vaccinia, and mumps.

The contagiousness of the infectious diseases is a matter of degree. It is probable that most if not all of the specific infections are transmitted from one individual to another. The degree of contagiousness depends upon the manner, ease and frequency, with which such transmission occurs. With each infection, modern medicine must concern itself largely with the mode of transmission.

In former times, descriptions of the specific infections were concerned almost exclusively with the symptoms, differential diagnosis, and symptomatic treatment of the diseases belonging in this group. Under the most modern views, we must consider two other aspects of a specific infection as of particular importance. The first of these aspects is the *manner of transmission and invasion*, that is, how the parasite is brought to the host, and how it gains access to the tissues of the host. The second of these aspects is the *defensive or "immune" reaction of the host against the invading parasite*. Upon these two aspects of the specific infections depend most of our prospects of progress in knowledge and in ability to combat these disease processes successfully.

Classification of the specific infections upon any definite scientific basis is impossible. For convenience of description, the following grouping will be employed:

- | | | |
|--|---|-----------------------------------|
| | { | Scarlet Fever |
| | | Measles |
| 1. The Exanthemata | | Rubella |
| | | Varicella |
| | | Variola |
| | | Vaccinia |
| | { | Diphtheria |
| 2. Highly contagious diseases without exanthem . . . | | Pertussis |
| | | Mumps |
| | | Influenza |
| | { | Typhoid Fever |
| 3. Diseases with constant infection of the blood . . . | | Malaria |
| | { | Epidemic Cerebrospinal Meningitis |
| 4. Diseases tending to occur in epidemics | | Polio-myelo-encephalitis |
| | { | Rheumatic Fever |
| 5. Diseases of doubtfully specific cause | | Erysipelas |
| | { | Tuberculosis |
| 6. Diseases essentially chronic | | Syphilis |

I. THE EXANTHEMATA

In contradistinction to the various diseases of the skin which dermatologists are accustomed to designate as exanthems of local origin are certain acute diseases characterized by exanthems symptomatic of the specific infection, which are called the exanthemata. This group of infectious diseases is of especial interest in connection with children, as it is among children that they most frequently occur. They can, however, attack individuals of any age. Although none of these diseases is entirely self-protective, yet the instances in which they develop in an individual more than once are rare. Each of these diseases is characterized by certain conditions common to all. Besides being highly contagious, each disease runs a definite course and is self-limited, facts which should be remembered in the study of its diagnosis and treatment.

The course of these exanthemata from the time when the infection takes place up to the appearance of their later manifestations may be divided into distinct stages. In the first of these a more or less definite period elapses between the acquirement of the infection by contact, and the appearance of any disease manifestations. During this period the infecting organisms apparently remain dormant for a time, constituting what is called the *stage of incubation*. The stage of incubation is followed by certain general symptoms resulting from the supposed development of the special organisms and constituting the *prodromal stage*, or stage of invasion. These prodromal symptoms are, after intervals varying according to the special disease, followed by an efflorescence on the skin, which marks the third stage of the disease, called the *stage of efflorescence*. The efflorescence in its turn is followed by what is called the *stage of desquamation*, this desquamation being more or less pronounced in proportion to the intensity of the lesions of the skin which have occurred during the stage of efflorescence.

SCARLET FEVER

(Scarlatina)

Scarlet fever is a specific infectious disease, characterized by angina, exanthem, and a tendency to certain special complications. It is contagious, self-limited, and one attack confers an immunity which usually protects the individual throughout life.

ETIOLOGY. THE MICROÖRGANISM. — The organism which causes scarlet fever is unknown. In the necrotic tissue and inflammatory

exudate of the throat is found almost always a streptococcus. The same type of organism has been found in the blood, not only in severe and fatal cases, but also in blood cultures from mild cases. These findings have led some writers to regard this streptococcus as the cause of the disease. Favorable reports on the effect of both streptococcus vaccine and antistreptococcic serum in the treatment of scarlet fever have lent additional weight to this theory, and some investigators have even reported biological differences between the streptococcus found in scarlet fever and other strains of streptococci. Nevertheless, although scarlet fever has been successfully transmitted to the anthropoid apes, all attempts to produce the disease experimentally with streptococcus cultures have failed. There is much other evidence against the streptococcus origin of scarlet fever, such as the peculiar contagiousness of the disease, the immunity conferred by one attack, and the fact that the streptococci are usually not found in the earliest stage of the disease. Most authorities believe that these streptococci represent a secondary infection, which, however, may have an important influence on the course and complications of the disease.

Within the last few months, Mallory has reported the finding of an organism, which he believes may prove to be the specific cause of scarlet fever. This organism is a bacillus which in appearance somewhat resembles the bacillus of diphtheria. The evidence in favor of its etiological importance is its constant presence in the deeper layers of the tonsillar tissue in scarlet fever, and its absence in other cases. At the present writing, inoculation experiments are being conducted with cultures of this organism, the outcome of which will probably decide the question of its relation to scarlet fever.

TRANSMISSION.—Every case of scarlet fever comes from some other case, the disease being transmitted from a sick to a healthy individual. The virus cannot, however, as many persons suppose, fly through the air across a considerable space. Under ordinary circumstances the mere coming into a room occupied by a scarlet fever patient, provided that nothing in the room be touched, would not be a sufficient exposure to cause infection. The usual means of infection in scarlet fever is *actual contact with infected material*. Infectious material from the patient, such as secretions from the mouth and nose, reach the outside world where it can contaminate any object with which it comes in contact. It most often reaches the healthy individual through *direct contact*, such as occurs in kissing, or handling, or sleeping together. In addition to direct contact, *indirect contact* plays an important rôle in scarlet fever. In this mode of transmission, healthy persons, and various objects, such as handkerchiefs, food, toys, carpets, and so forth, become contaminated by the patient, and constitute the carriers of the disease. This in-

direct contact, while much less common than direct contact, is nevertheless important in scarlet fever, because the virus is able to retain its infecting power for a considerable time outside the human body.

There is a possibility of transmission through the air without actual contact, the virus being carried in the fine, moist particles expelled in sneezing and coughing. In scarlet fever, however, this plays a very slight part, and is not likely to occur unless the patient cough directly in the face of the exposed child.

THE INFECTIOUS PERIOD.—Scarlet fever is contagious from the very beginning, possibly even a day or two before the appearance of symptoms. It was formerly supposed that it was not contagious in the prodromal stage, but it is now regarded as *certainly contagious from the appearance of the first symptom*. The spread of the disease is largely due to mild ambulant, or unrecognized cases. The duration of the contagious period is long, and probably very variable. It has long been known that scarlet fever is usually contagious throughout the stage of desquamation, the average duration of which is about six weeks. It has been wrongly considered that the contagious period necessarily ends with the completion of desquamation. Under this view, the scales of desquamation were considered a source of infection. There is, however, no definite evidence that the scales contain the virus, and those instances in which the disease has apparently been transmitted by the desquamating particles of epidermis can be explained on the ground that the scales became contaminated by secretion from the mouth or nose. We cannot say with absolute certainty that the scales are not contagious, but the weight of evidence is decidedly against such a theory. Certain it is that there are cases on record in which the patient was discharged well after desquamation had been completed, even as long as ten weeks after the onset of the disease, and still caused the infection of others.

Altogether too much attention has been paid to the scales of desquamation. The chief danger comes from the secretions and discharges of the patient, which have been proven to be infectious. Early infection probably occurs simply from the secretions of the mouth and nose, while the later infection in the stage of desquamation may come from the discharges from otitis, rhinitis, suppurating glands and so forth.

The infectious period of scarlet fever being variable, and there being no means of determining whether the patient is still a possible source of infection, some definite limit must be assigned, for the purpose of isolation and the protection of others. The contagious period of scarlet fever has been arbitrarily placed at six weeks by most writers. While the majority of children are not capable of infecting others after six weeks, I believe this period to be too short for the purpose of complete protection. Certainly no patient who has any visible discharge from the mucous membranes should be

released from isolation, even if six weeks have elapsed and desquamation has been completed. I would not allow my own patients to receive in their homes, or to play with any child who has just been discharged from scarlet fever isolation at the end of six weeks, but in order to take every possible precaution, would require the lapse of ten weeks.

THE PORTAL OF ENTRY.—The route by which the virus of scarlet fever enters the body has not been established by certain proof. The weight of evidence however, is strongly in favor of the throat as the first localization of the infection, which points to the mouth as the probable portal of entry.

THE INCUBATION PERIOD.—The period of incubation of scarlet fever is variable, but is short in comparison with the other exanthemata. In the great majority of cases it is less than seven days. The commonest period is *from two to four days*.

PREDISPOSITION—Scarlet fever may occur at any age. It is very much commoner in childhood than in adult life. The commonest period of occurrence is from three to six years of age. Susceptibility continues to be marked up to about the age of thirty years, after which it diminishes. The disease is rare in the first year of life, especially in the early months.

The following table was compiled by McCollom. It represents the age and the number of deaths in one thousand cases of scarlet fever treated in the contagious wards of the Boston City Hospital:

TABLE 48

One Thousand Cases of Scarlet Fever, by Ages, With the Deaths

YEARS	CASES	DEATHS	YEARS	CASES	DEATHS
Under 1 year.....	9	2	19 years.....	10	1
1 year.....	24	8	20 years.....	7	0
2 years.....	66	20	21 years.....	8	3
3 years.....	115	21	22 years.....	8	0
4 years.....	99	7	23 years.....	15	0
5 years.....	124	9	24 years.....	9	0
6 years.....	106	7	25 years.....	7	0
7 years.....	64	6	26 years.....	5	0
8 years.....	62	5	27 years.....	7	1
9 years.....	58	1	28 years.....	6	1
10 years.....	53	3	29 years.....	3	0
11 years.....	21	1	30 years.....	9	0
12 years.....	20	0	31 years.....	3	0
13 years.....	23	1	32 years.....	3	0
14 years.....	10	0	33 years.....	2	0
15 years.....	12	0	34 years.....	3	0
16 years.....	10	0	35 years.....	1	0
17 years.....	7	0	41 years.....	0	0
18 years.....	9	1	50 years.....	1	0
				1000	98

The predisposition of children toward scarlet fever is much less than toward measles and whooping-cough. In the most severe epidemics, not more than twenty per cent of the exposed who had not had a previous attack, including adults, contracted the disease, while about fifty per cent of the children escaped. In families with numerous children, there are often only one or two cases, whereas with measles or whooping-cough all are usually affected.

This peculiarity of the predisposition of children to scarlet fever has usually been explained on the ground of a varying individual susceptibility to the infection, some children having a natural immunity. I do not believe this explanation to be correct, but believe that the apparently varying susceptibility depends on the method by which scarlet fever is transmitted. Measles and whooping-cough are not contact infections, but what the German writers call "drop-let infections" (tröpfcheninfektion), in which the virus is carried through the air by the moist particles expelled in coughing, and these particles can traverse a very considerable air space. In a contact infection such as scarlet fever or diphtheria, the acquirement of the disease depends on whether or not the virus is properly carried to the exposed child, and all sorts of irregularities in the carrying over of the virus into the required contact are possible, which irregularities might easily cause the apparent variations in susceptibility. In other words, I believe that the exposed children who escape do not come in contact with the virus, which consequently never reaches the portal of entry. This theory is fully adequate to explain the known facts, and I believe it to be more in harmony with them than the theory of natural immunity. The latter theory could only be proved by the impracticable method of actually inoculating a series of healthy children.

Similarly, it is generally supposed that the greater frequency of scarlet fever in childhood is due to the fact that children are more susceptible than are adults. Even when those adults are excluded who are protected by a previous attack, scarlet fever is much more likely to attack children than unprotected adults, but I do not believe that this is due to a greater susceptibility in childhood, or that adults acquire a relative immunity. I believe that the frequency of scarlet fever among children is also to be explained by the mode of transmission of the disease. *Close contact* is a condition much commoner in childhood. Children live close together, often sleep together, play together, and are often assembled in groups, as in school and kindergarten. Children are often habitually uncleanly with their secretions, which soil their faces, hands, beds and clothes. All the conditions favoring the spreading of a contact infection such as scarlet fever are multiplied in childhood, and this I believe to be the true explanation of the greater frequency of the

disease at this age. Whether or not the rarity of the disease in the first year is due to less opportunity for effective contact, or to a natural immunity, it is impossible to say.

IMMUNITY.—An attack of scarlet fever confers a pronounced and lasting immunity. Nevertheless, second attacks, though rare, are seen at times, and are commoner than in measles.

PATHOLOGICAL ANATOMY.—The only constant and characteristic lesions of scarlet fever are found in the skin, in the mouth and throat, and in the lymphnodes.

THE SKIN.—The lesion of the skin in scarlet fever is an acute dermatitis, of variable depth and intensity. The process goes through the stages usual in acute inflammation, first hyperemia, then exudation of serum and cells into the corium, then death of the epidermis, which is cast off in flakes.

The changes in the mucous membrane of the mouth are similar to those in the skin, the inflammation taking a catarrhal form. It frequently extends to the nose and middle ear, from which places in turn it may invade the mastoid cells or the accessory sinuses. It rarely invades the larynx.

THE THROAT.—Superficially the mucous membrane of the throat may show nothing more than an intense redness, suggesting only a catarrhal inflammation. In reality, however, the inflammatory process in the scarlet fever angina is much deeper, particularly in the tonsils and adjacent mucous membrane. It is always really a phlegmonous inflammatory process which tends toward a certain amount of purulent softening, and which extends deeper into the tissues than does the inflammation of diphtheria, although it often does not present such characteristic appearances on the surface. In the more severe cases the inflammation may produce a coagulation necrosis, which gives the appearance of a gangrenous or membranous angina which superficially resembles the lesion of diphtheria. The false membrane in scarlet fever is usually found filled with streptococci. It is in the deeper layers that Mallory has found his bacillus. The necrosis may be more or less extensive over the mucous membrane of the throat, and the inflammation may extend to the cervical lymphnodes, causing purulent softening. It is the streptococci which are concerned in this latter process.

THE LYMPHNODES.—The most constant change throughout the body in scarlet fever is a hyperplasia of all the lymphoid tissue.

TOXIC LESIONS.—The poison of scarlet fever may produce a variety of lesions in the various parenchymatous organs of the body, which do not differ from the lesions associated with other varieties of toxemia. The one particularly associated with scarlet fever is an acute toxic nephritis. Among the toxic lesions seen in fatal cases

are fatty degeneration of the myocardium, focal necrosis of the liver, and proliferation of the cells of the Malpighian bodies of the spleen.

SECONDARY LESIONS—The streptococcus infection may extend to various parts of the body, causing secondary lesions. Beside otitis media and purulent cervical adenitis, secondary lesions which may occur at times are bronchopneumonia, pleurisy, abscess of the lung, endocarditis, pericarditis, arthritis, and abscesses in the cellular tissue.

THE TYPICAL FORM OF SCARLET FEVER

PRODROMAL STAGE OR STAGE OF INVASION.—The invasion of the disease is usually sudden, and, as a rule, active. The child feels very sick, looks dull, and in a large number of cases vomits continuously. The vomiting usually ceases in the stage of efflorescence and often before the prodromal stage has ended. The pulse is rapid. The temperature is high, 103° , 104° , 105° F. In infants and very young children if the temperature rises to 104° or 106° F., convulsions are very likely to occur. Older children complain of sore throat, and often of headache. Young children show marked apathy or restlessness, and often are delirious.

At this stage the physician finds nothing on physical examination which can account for the high fever and toxic symptoms, except in the throat. The appearance of the mucous membrane of the throat, although perhaps not characteristic, as at times a simple non-specific pharyngitis may simulate it quite closely, is, in connection with the general symptoms, at least suggestive. The mucous membrane of the soft palate and of the pharynx is much congested. The redness covers the soft palate only, being sharply bounded at the hard palate.

In this stage, a positive diagnosis of scarlet fever cannot be made, but the symptoms and appearance of the throat should always arouse suspicion.

EFFLORESCENCE—The prodromal stage in scarlet fever is comparatively brief, and the efflorescence usually begins to appear in from twelve to twenty-four hours after the onset. It appears first on the neck, chest, or back, and next extends over the entire trunk, and to the upper arms and thighs. Finally it reaches the forearms, legs, hands, and feet. The full extension of the eruption occupies about two days, at the end of which time the entire body is involved with the exception of the face. The cheeks may be reddened, but the redness is a simple congestion, not the punctate rash of scarlet fever. The nose, upper lip, and chin remain entirely free, even from reddening, and this pale area shows a marked contrast to the redness of the skin elsewhere, and is a characteristic symptom of scarlet fever.

The eruption is a punctate erythema, which becomes confluent. The first appearance is that of scattered, very small, light red spots, between which the normal skin is clearly visible. Between the punctate spots new ones keep appearing, until after one or two days, they become confluent. In the meantime the eruption has been constantly becoming a brighter red, until at the time of full development, the skin presents a brilliant erythematous blush, which does not appear to be made up of single punctate spots, except in certain situations such as the inner surface of the thighs, and the backs of the hands. At all times pressure with the fingers will cause disappearance of the exanthem, and when the pressure is released, even if the rash is in the confluent stage, the discrete punctate spots will reappear first, and then rapidly become confluent.

In the early stage of the efflorescence, the punctate spots are flat. With full development they become slightly raised, so that on stroking the skin with the finger, a very fine unevenness is detected. The swelling of the follicles in the regions of the forearms, lower legs, and backs of the hands and feet, sometimes causes the formation of larger papules. Sometimes the papules become slightly vesicular. These variations of the rash have no relation to the severity of the case. Very small hemorrhages may sometimes be seen in those regions where the clothing binds or chafes, such as the elbows or the axillae. The eruption sometimes itches.

The efflorescence reaches its height in from three to five days, and then gradually disappears in the order of its appearance. It is usually entirely gone by the beginning of the second week. A certain amount of pigmentation of the skin may persist.

DESQUAMATION.—The stage of desquamation begins at about the seventh day from the time when the efflorescence first appeared and on the parts of the skin first attacked. The desquamation, however, is not always proportionate to the intensity of the efflorescence. It is at first composed of small particles of cutis, but these soon become larger, and early in the third week from the beginning of the disease they fall from the body in large flakes, and are most characteristic and pronounced on the fingers and toes. This form of desquamation is called *lamellar*. Here, again, we have an important means of distinguishing scarlet fever from measles, for in measles the desquamation is almost universally of a furfuraceous character throughout the whole course of the disease, while the characteristic desquamation of scarlet fever is lamellar. This lamellar form of desquamation may, at times, in certain individuals, and following more intense inflammation of the skin, be represented by large and extensive pieces of skin. This is well shown in a specimen in the Warren Museum, where large strips of skin have come from the hand of a patient with scarlet fever so as almost to form a glove.

PLATE VIII.



Scarlet Fever.



Measles.

Sometimes the desquamation lasts only ten days, but it usually continues for two or three weeks, and may not be complete for six or eight weeks. It is especially slow in disappearing from the hands and feet, and it may remain between the fingers and toes for a number of weeks. Sometimes after the desquamation has apparently ceased, and the skin has been smooth and normal for several days, it may begin again, and thus prolong the period of convalescence.

THE MOUTH AND THROAT.—The redness and swelling of the tonsils, soft palate and pharynx which is present during the stage of invasion, increase for the next three or four days during the stage of efflorescence. Older children complain of sore throat, while in younger children pain on swallowing is often evident. The color of the throat is a fiery red, of an intensity seldom seen in ordinary pharyngitis or tonsillitis. The swollen tonsils often show yellowish exudate in the crypts. The submaxillary lymphnodes are enlarged, and usually tender to pressure. In typical cases the scarlet fever angina reaches its height in from three to five days, after which it gradually improves, but a membranous type may develop even after this time.

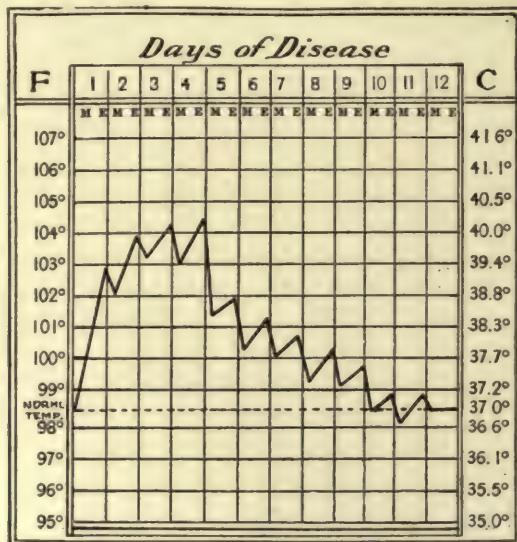
The tongue in the stage of invasion is heavily coated, but clears rapidly during the stage of efflorescence, and by the third or fourth day shows a bright red surface on which the enlarged papillae stand out prominently. This is the characteristic "strawberry tongue" of scarlet fever, which has been considered diagnostic by some writers. It is an aid in diagnosis, but is sometimes seen in other conditions, and is occasionally lacking in scarlet fever.

THE TEMPERATURE.—The fever continues high, 103° F., to 105° F., for the first three to five days of the disease, and often mounts steadily higher until the full development of the exanthem. The height of the temperature depends more upon the severity of the angina than upon the intensity of the efflorescence. After the full development of the rash, the temperature begins to fall by a step-like lysis, reaching the normal from the seventh to the tenth day. Occasionally in cases otherwise typical, the fever may persist as long as two weeks, without any discoverable cause or complication to account for its persistence.

THE PULSE.—In scarlet fever the pulse is very rapid, the acceleration in children being greater than would ordinarily be accounted for by the temperature. Younger children often have a pulse rate of from 160 to 180 in typical mild cases. Increase in pulse rate persists after the temperature has fallen to normal, and disappears gradually.

THE GENERAL CONDITION.—Apathy, restlessness, sleeplessness, weakness, and anorexia are common symptoms accompanying the fever, and disappear as the temperature falls. Vomiting usually ceases during the stage of efflorescence. The nose and conjunctivae are not notably affected, and the ears are usually not involved during the stages of invasion and efflorescence. All the palpable lymph-nodes are noticeably enlarged, and the tenderness of the cervical lymphnodes may make movement of the head painful.

CHART 6



THE BLOOD—The blood shows regularly a leukocytosis, the white count being between 18,000 and 40,000. The increase is entirely in the polymorphonuclear neutrophils. The leukocytosis gradually disappears in the second or third week. There is often, but not always, a diminution of the eosinophiles, beginning at the end of the first week. Certain inclusion bodies, first described by Döhle, are regularly found in the leukocytes during the febrile stage. They were at one time considered diagnostic, but have been shown to be present in other acute infections.

THE URINE—The urine is lessened in amount during the febrile period, returns to normal amount after defervescence, increases during the stage of desquamation, amounting at times to polyuria, and returns again to the normal amount at the end of this stage. During the stage of efflorescence, especially if the temperature is considerably heightened, there may appear in the urine a small amount of albumin, and a few casts and red blood cells, but these disappear as

the temperature subsides, are probably only the result of the fever, as in many other diseases accompanied by a high temperature, and their appearance is not to be confounded with the albuminuria of the nephritis which in some cases complicates the stage of desquamation. Acetonuria is often seen in scarlet fever, especially in younger children.

CONVALESCENCE.—All the symptoms subside with the fall of the temperature. The patient appears fully convalescent by the middle or end of the second week, often before desquamation has begun.

· ATYPICAL FORMS OF SCARLET FEVER

The form of scarlet fever described above as typical, is the commonest. It represents a medium or average severity of the disease. Deviations from this typical form are, however, extremely common, both on the mild side and on the severe side. In fact they are so frequent that the term atypical is hardly suitable.

THE MILD FORM.—Very mild cases of scarlet fever are quite common, and at certain times the majority of cases in any locality may be of the mild type. Their recognition is important, as they are often largely responsible for the spread of the disease.

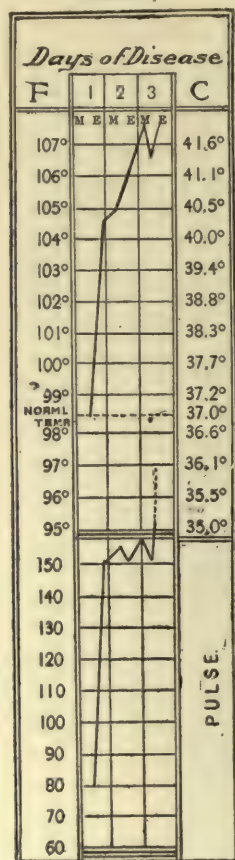
In the mild type the sore throat, fever, and constitutional disturbances are very slight, often not enough to attract attention. In such cases the only symptom noted by the child's parents may be the efflorescence. The temperature may not go above 101° F., there may be no sore throat, and the child does not feel sick enough to want to go to bed. Even the efflorescence itself may be very slight, appearing only on part of the body at a time, and never becoming confluent. Sometimes even the rash is overlooked, and the disease runs its course unsuspected, until the appearance of desquamation, or of a nephritis, arouses suspicion that scarlet fever has gone before. Even the desquamation, especially in children who are bathed daily, may be overlooked, unless special note be taken of the appearance of the fingers and toes.

THE "RUDIMENTARY" TYPE.—In this type the angina, fever, and constitutional disturbance are typical, but the efflorescence is very slight, or even absent. The rash may not appear till the third, fourth, or fifth day, and is slight in intensity, and limited in distribution. It is usually most pronounced on the back. Cases without any rash are seen occasionally in older children and adults. These rudimentary forms resemble ordinary tonsillitis or pharyngitis, and are known to be scarlet fever only through simultaneous occurrence with other cases in the family.

SEVERE FORMS.—The most severe type, sometimes called *malignant scarlet fever*, is comparatively rare. The child is suddenly

attacked with high fever, vomiting, often convulsions, delirium, or unconsciousness. The breathing is deep and toxic, the pulse is intermittent and scarcely perceptible, there is slight cyanosis, and the extremities are cold. The throat shows the usual scarlet fever angina, but the skin shows no rash characteristic of scarlet fever. Some times purpuric spots are present. Death usually occurs in from

CHART 7



Malignant form of scarlet fever. Girl, 11 years old

twenty-four to forty-eight hours. If the patient lives a day or two longer, the angina becomes more marked, the lymphnodes enlarge, and the scarlet fever rash begins to appear, but usually involves only parts of the body. This severe type is contracted from patients having a milder type, and is apparently due to some constitutional peculiarity or predisposition on the part of the patient.

The most common severe type is much less fatal than the malignant, and is the form usually associated with a *membranous angina*.

The severe symptoms are not, as in the malignant form, due to the scarlet fever contagion, but to the *associated secondary streptococcus infection*. The onset is severe, with high fever, marked constitutional disturbances, and severe angina. The efflorescence runs the ordinary course. About the third or fourth day, however, the throat, instead of showing the usual appearance of catarrhal inflammation, or follicular tonsillitis, takes on the appearance of membranous angina. Part or all of the tonsils becomes covered with a white or greyish-white false membrane, which at first closely resembles the membrane of diphtheria. After a time, the membrane appears more adherent, and more deeply implanted in the mucous membrane, than does that of diphtheria. The membrane frequently spreads to the soft palate and pillars, and occasionally to the posterior pharyngeal wall. In the meantime the enlargement of the cervical lymph-nodes becomes very marked, and the inflammation often spreads to the adjacent connective tissue, making movement of the head painful, and sometimes forming a hard swelling on each side of the neck. This phlegmonous inflammation may be so marked, that the swellings on the two sides meet under the chin. The membranous inflammation often extends into the nasopharynx, and can begin there. This causes obstructed nasal breathing, and a purulent discharge.

In favorable cases the membrane begins to disappear in from five to eight days after the onset, and the fall of temperature by lysis occurs. In bad cases the tissue necrosis becomes deeper, and the tissue of the tonsils, and often of the adjacent parts, breaks down, forming a brownish ulceration, covered with a bloody-purulent discharge. The process occasionally extends to the epiglottis and into the larynx, causing stenosis.

Continued fever and marked constitutional disturbance attend the development and spreading of the membranous angina. The course of these severe cases depends upon the variety and severity of the complications.

COMPLICATIONS.—The complications of scarlet fever which occur in the early stages of the disease are due to the extension of the associated secondary streptococcus infection to various parts of the body. All these complications may occasionally occur in the course of a typical mild case of scarlet fever. The disease may run what is apparently a normal course for a time. The temperature may begin to fall, and then suddenly rise again, without it being immediately clear what is the cause. In such cases careful examination will eventually disclose that the patient has developed either a membranous angina, or some other complication.

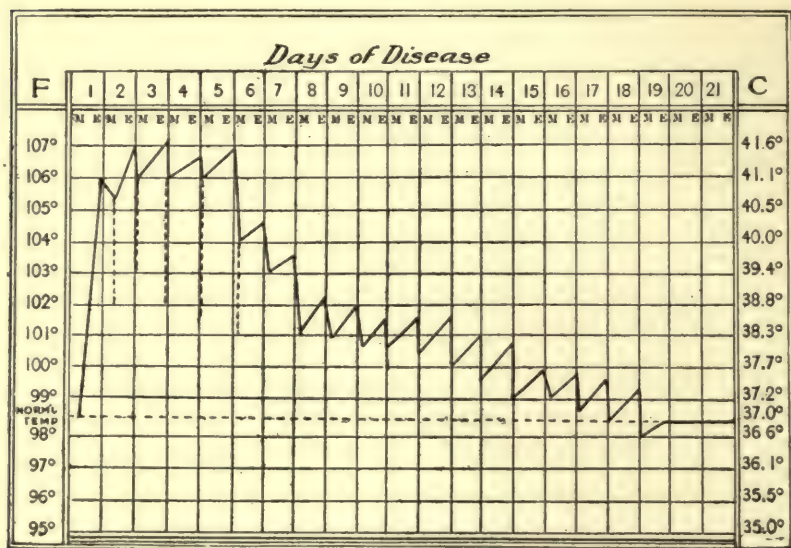
While the various complications due to secondary streptococcus infection may occur in cases otherwise apparently typical, they are

most commonly seen in cases which have either shown a membranous angina from the start, or which have developed a membranous angina.

THE LYMPHNODES.—The acute inflammation of the lymphnodes and surrounding cellulitis, may go on to suppuration. The infection may extend to the mediastinal lymphnodes, causing a purulent mediastinitis, and eventually leading to general sepsis, with metastatic abscesses in various parts of the body.

THE EAR.—The middle ear is so closely connected by means of the Eustachian tubes with the naso-pharynx, that aural complications are exceedingly common. The symptoms which indicate that a secondary infection of the ear is taking place are not always clear, as they may differ much in their manifestations. We should there-

CHART 8



Toxic symptoms and high temperature in scarlet fever treated by baths

fore watch with the greatest solicitude and examine the ear with the greatest care during the course of scarlet fever. The symptoms may be active and represented by aural pain and great restlessness. On the other hand, there may be no apparent pain, especially in infants and young children, who are often unable to indicate the location of the pains by which they are affected. In these cases the symptoms may be merely a somnolent condition and occasional attacks of fretfulness.

Cases of scarlet fever occurring in the fall and winter are much more likely to develop middle ear complication than at other seasons. When it does occur, both ears are usually affected early in the second week. If the constitutional symptoms of the primary

disease are severe, no new symptoms show themselves, so that the ear complications may be easily overlooked until much damage has been brought about. The otitis is purulent, and much of the membrum tympani is usually destroyed. Mastoiditis and septic sinus thrombosis are not very rare. The scarlet fever otitis has the peculiarity that it occasionally produces necrosis of the ossicles, and sometimes more widespread necrosis. This results in impaired hearing or deafness. May has shown by statistics that of 5613 cases of deaf-mutism, 572 were due to scarlet fever. The absence of symptoms pointing to the ear does not, therefore, justify us in overlooking an otitis media. Routine examinations of the ears should be made in all cases.

THE JOINTS.—An acute inflammation of the joints, usually the larger ones, is not infrequently met with during the course of scarlet fever. It is more frequent in adults than in children, and usually occurs at the end of the first week. As a rule, these cases are not of long duration, and if effusion takes place in the joints it is serous, does not become purulent, and does not give an especially serious prognosis.

A more severe form of arthritis, apparently caused by secondary infection with streptococci, may also occur during the course of scarlet fever. The effusion into the joints in these cases becomes purulent and leads to serious and permanent disorganization of the tissues and often to death from general septic infection.

THE HEART.—The rapid pulse which is seen as a rule in scarlet fever shows that the heart is particularly susceptible to the toxin of the disease. In severe cases this rapid pulse persists after the end of the febrile period, and is sometimes accompanied by other signs of cardiac weakness.

In addition to this toxic manifestation, a cardiac lesion sometimes complicates scarlet fever. It usually appears at the end of the first or in the second week of the disease. The commonest manifestations are a systolic murmur at the apex, enlargement of the cardiac dulness to the left, and sometimes bradycardia. These symptoms can last several weeks, but finally disappear entirely. They are due not so much to a true endocarditis, as to an atony of the heart muscle with slight dilatation and relative mitral insufficiency.

A true endocarditis, however, can also complicate scarlet fever, and cannot be distinguished from the condition just described. Occasionally it is ushered in by a reappearance of fever. In such a case the mitral murmur is permanent.

Pericarditis is rare.

THE LUNGS.—Scarlet fever may be complicated by purulent bron-

chitis, bronchopneumonia, and empyema. These complications are, however, comparatively rare.

SEQUELAE.—Most of the complications described above occur comparatively early in the course of the disease. Occasionally, however, between the end of the second week and the sixth week, a reappearance of fever is observed, which is found to be due to the late development of fresh lymphnode infection, otitis, arthritis, or endocarditis. Rarely is seen an actual scarlet fever relapse, with a fresh appearance of angina and efflorescence.

NEPHRITIS.—This is the most common and important of the sequelae of scarlet fever. It usually appears in the third week of the disease, almost never before the twelfth day, and often not until the fourth, fifth, or even the sixth week. It is a toxic nephritis, the glomeruli chiefly being affected. The advent of nephritis is most commonly recognized by the appearance of edema and bloody urine, although if the physician examines the urine daily, he can sometimes discover an approaching nephritis before the appearance of edema. Occasionally the development of nephritis is heralded by fever, vomiting and headache, but more often edema is the only symptom noted. The urine is much diminished in quantity, and sometimes, in severe cases, anuria is seen. The urine usually contains considerable blood, and in color is red or "smoky." There is usually a rather large quantity of albumin, while the sediment shows numerous red blood corpuscles and casts. The edema begins about the eyes, and usually involves the skin of the whole body. Fluid is often found in the peritoneal cavity, the pleural cavities, and the pericardial cavity. Enlargement of the area of cardiac dullness, bradycardia, and raised blood pressure appear in a short time. In cases with anuria, or marked diminution in the amount of urine, headache and vomiting may appear, followed by slow pulse, convulsions and coma.

In most cases the scarlet fever nephritis is completely healed after five or six weeks, or somewhat longer. In some cases chronic nephritis may persist. In still less common cases, death may occur either from uremia, or from increasing edema and dilatation of the heart.

The frequency of nephritis is very variable at different times, and in different epidemics, the incidence being from 2 per cent. to 30 per cent. The development of nephritis also appears to bear no relation to the severity of the scarlet fever.

DIAGNOSIS.—In typical cases of scarlet fever the combination of fever, characteristic angina, efflorescence and strawberry tongue, makes the diagnosis easy. The diagnosis cannot be made with certainty before the appearance of the rash. Every case of sore

throat in a child should at the start be regarded as a possible case of scarlet fever, and the patient should be isolated. The appearance of the throat may or may not be sufficiently characteristic to render the suspicion of scarlet fever very strong. Fortunately, the prodromal stage is so short, that the appearance of the rash will confirm the suspicion within twenty-four or thirty-six hours, if scarlet fever be present.

It is the frequent occurrence of atypical cases, particularly the mild and rudimentary types, which makes the diagnosis of scarlet fever difficult. In many cases the physician cannot be sure whether he is confronted by an atypical case of scarlet fever, or by some other condition. Cases of scarlet fever without exanthem are rare, and can only be recognized by their occurrence in association with other cases to which the patient has been exposed. But in the mild and rudimentary types, the efflorescence may be atypical and fleeting, and the diagnosis may remain doubtful. In this connection, however, it is well to remember that *a scarlatiniform rash which is visible for only twenty-four hours or less, is usually not scarlet fever.*

The usual problem in diagnosis which presents itself to the physician, is whether a certain rash or efflorescence on the skin represents scarlet fever or not. Many diseased conditions may be accompanied by a cutaneous rash which resembles more or less closely the efflorescence of scarlet fever. When a definite angina is present, together with fever and constitutional disturbance, the evidence points toward scarlet fever. When, however, fever and angina are slight, particularly if the efflorescence be not general, the diagnosis is much more difficult.

The following are conditions which are with difficulty differentiated from scarlet fever:

Toxic Erythema.—This is seen in a number of conditions in childhood, particularly in cases of disturbed nutrition and metabolism. The rashes which occur after the administration of certain drugs, and the serum rashes, belong in the same class. As compared with scarlet fever, these rashes are more fleeting, and often show a changing character, so that cutaneous lesions resembling urticaria or measles are seen alongside of the scarlatiniform eruption. Furthermore, angina is absent in these erythemas, the throat appearing normal. Fever and constitutional disturbance are slight or absent. The leucocytosis characteristic of scarlet fever is absent, and, especially in serum rashes, there is apt to be leukopenia, with relative diminution of the polynuclear forms.

Infectious Erythema.—An erythematous rash may appear as a symptom of a variety of acute infections. It is usually not made up of the punctate areas characteristic of scarlet fever. Angina is

absent. The recognition of the underlying infectious process is of aid in the diagnosis. The most common infections which sometimes produce a rash in children, are lobar pneumonia, typhoid fever, and influenza.

Measles.—Scarlet fever and measles should easily be differentiated. The long prodromal stage, the catarrhal symptoms and conjunctivitis, the Koplik's spots, the absence of characteristic angina, and the different appearance of the efflorescence, differentiate measles so completely that one rarely has to think of it in diagnosis. The rash of measles is characterized by larger macules; if larger macules are seen in scarlet fever, they are never general, but are usually confined to the extremities. The measles rash involves the cheeks, nose and chin. If it is so confluent in places as to resemble the appearance of scarlet fever, there are always other parts of the body where the macules of measles are discrete and typical.

Rubella and "Dukes' Disease."—Typical German measles, with the larger macules which never become confluent, should never be confused with scarlet fever. It is a question whether the condition described by the German writers as "Dukes' Disease" or "Fourth Disease," represents a distinct specific infection, or whether it is a type of German measles with scarlatiniform rash. The efflorescence resembles scarlet fever, but angina is absent, and fever and constitutional disturbance are slight. Mild cases of scarlet fever have the same characteristics, and Dukes' Disease is difficult to distinguish from such cases. The "strawberry tongue" is absent in "Dukes' Disease," and desquamation does not occur. The disease is rare.

Miliaria.—In infants and young children who are too warmly dressed, and who sweat freely, there occurs a punctate rash, popularly called "prickly heat," which superficially bears a close resemblance to the scarlet fever exanthem. When it is localized, the distinction is not difficult, but miliaria may involve the entire body. It is recognized by the prominent raised character of the rash, which gives it a peculiar rough or prickly feeling. The absence of angina and the other symptoms of scarlet fever strengthens the diagnosis of prickly heat.

Diphtheria.—The membranous angina of scarlet fever may suggest diphtheria, but the latter disease is recognized by the absence of a cutaneous efflorescence, and by the presence of the diphtheria bacillus in culture from the throat.

PROGNOSIS.—In mild and typical types of scarlet fever, the prognosis is favorable. In the severer types with membranous angina the prognosis is more doubtful, depending on the severity of the case, and on the number and character of the complications. The

violence of the invasion and severity of the constitutional disturbance at the onset is some indication as to the severity of the case, but even in cases with a comparatively mild invasion, the physician should always give a guarded prognosis, because in no disease is the course to be reckoned with less certainty than in scarlet fever. Mild cases may suddenly become severe, and unforeseen complications may develop at any time.

Every variation from the typical temperature curve is an unfavorable sign, and every rise in temperature after the fall by lysis has begun or after the temperature has reached the normal, should be regarded with suspicion, as it may mean a troublesome or dangerous complication or sequela.

The severity of the disease varies greatly in different epidemics, and at different times, so that the mortality varies between 1 per cent and 50 per cent. The average mortality is about 15 per cent. Children between the ages of two and four years are most in danger. Mild and typical cases, in which no membranous angina develops, are usually soon out of danger, without any treatment. In severe and toxic cases, the physician is practically powerless.

PROPHYLAXIS.—We must remember the fact that when the child has passed its tenth year the chances of its ever contracting the disease are very much lessened. We should, therefore under all circumstances discountenance the opinion so often expressed by the laity, and sometimes even by physicians, that it is well for children to have scarlet fever while they are young, on the ground that otherwise they will probably contract it at a later period of life, when the type of the disease may be more severe. The assertion that the type of the disease is more severe in adults than in children is not corroborated by my experience. Scarlet fever is so uncertain in its course, that it constitutes a very real danger, and every effort should be made to prevent exposure.

Isolation is the only effective prophylactic measure. As soon as there is any suspicion of scarlet fever, and throughout the course of the disease, the child should be strictly isolated with its nurse. Whenever conditions in the home prevent strict isolation, the child should be sent to a hospital.

An upper room should preferably be chosen, having its own bathroom. If possible a second room communicating with the sick room should be set apart for the nurse to change her clothes, and the physician to put on his gown. A disease which renders confinement to the room necessary for weeks demands a room with good ventilation and plentiful sunlight. Therefore, a room on the sunny side of the house, having an open fireplace, should be selected. The room should be free from all cotton or woollen materials except such as

can be destroyed by fire at the end of the disease. The blankets, sheets, towels, and clothes can, of course, be disinfected, but it will save much ultimate trouble to remove the carpet and the curtains and replace them with pieces of old carpet and sheets. The pictures, and, in fact, everything worth preserving, should be removed. The room can be made sufficiently cheerful by means of cheap colored prints and destructible toys to amuse the child.

During the whole course of the disease, the greatest care must be taken to disinfect the linen of both the patient and the nurse. This should be done by soaking it for twenty-four hours in a five per cent solution of carbolic acid, then boiling it for half an hour in water, and finally washing it with soft soap solution. All dishes and utensils which enter the sick room should be thoroughly washed before leaving it, and should be boiled as soon as they are taken down stairs.

Isolation should be continued until at least six weeks have elapsed. At the end of this time, if desquamation has entirely ceased, and if there is no discharge from the nose or throat, the patient may be released. The child is to be thoroughly washed: first in a solution of corrosive sublimate 1 to 10,000, then in water; it is then to be taken to another room to be wiped and put into fresh clothes, which have not been in the scarlet fever room. The mattress is to be tied up in canvas wet with a corrosive sublimate solution 1 to 500, and sent out of the house to be disinfected, if possible by steam. I usually advise the family never to have it brought back again. In place of the mattress it is far better to use old blankets, which, if in sufficient number, are comfortable, and at the end of the sickness can be thoroughly boiled and thus disinfected. The useless articles which have been in the room during the sickness should be burned in the open fireplace.

The room must next be disinfected. If there be paper on the walls, it should be scraped off and immediately burned. The floor should then be washed with a solution of corrosive sublimate 1 to 500, followed by soap water (a mop should be used so as to avoid irritation of the hands). The ceilings, the walls, all the woodwork, and the furniture are to be thoroughly rubbed with bread and then wiped with the corrosive sublimate solution 1 to 500. The room should then be thoroughly vaporized for eight or ten hours with formaldehyde. For every 3500 cubic feet of space, 250 grammes of formaldehyde should be used. This can be done with a vaporizing-lamp, the room first having been tightly sealed.

The room should then be aired for several days. If there are other children in the house, it is well to have the whole room painted, including the ceiling and the floor.

The physician should also bear in mind that the hair, beard, and

clothes are possible means of transmitting the contagium from one patient to another, and it is his manifest duty to the public to protect himself and others from the danger of carrying the contagium. It is best to wear a gown which extends from the neck to the floor, a cap with a flap to protect the hair, rubber over-shoes and rubber gloves. These articles are put on outside the sick-room and are discarded as one leaves the room. They are then left with the nurse and disinfected with corrosive sublimate and are kept outside the sick-room.

TREATMENT.—Scarlet fever is a self-limited disease, and there is no drug or therapeutic measure which can shorten the course of uncomplicated cases.

The scarlet fever patient should be put to bed at once. It is customary to keep even mild uncomplicated cases in bed for three or four weeks. This is done with the idea of avoiding nephritis, which often develops late. I do not believe, however, that nephritis can be avoided by keeping the patient in bed. In cases which run a mild or typical course, when the temperature has been normal for a week, and when the child seems fully convalescent, showing no evidence of complication, the patient may be allowed to get up. All cases in which any fever, rapid pulse, or any signs of complications persist, should be kept in bed till they have been thoroughly convalescent for at least a week, and show no more evidence of any infectious process.

The diet should consist of milk and farinaceous foods. Plenty of water should be given. After three weeks, eggs, broths and bread can be added to the diet, and after four weeks, a little meat, and from this time on the child can gradually return to its normal diet. The strict milk diet formerly prescribed is unnecessary, and it has been shown that nephritis is just as apt to develop as when the diet is more liberal. The cereal gruels can do no harm. When there is extreme anorexia, and it is difficult to get the child to take sufficient nourishment, it may be tempted by a more liberal diet.

Isolation, proper nursing, and proper diet being established, it is the duty of the physician to watch carefully for the various symptoms and complications which may require treatment. I have known physicians who actually contented themselves with watching the progress of the efflorescence, which is of no importance whatever in the care of scarlet fever. The important things, which should be examined and noted at each daily visit, are the *temperature, the throat, the ears, the cervical lymphnodes, and the heart*. Any rise of temperature, or departure from the normal temperature curve, which is not explained by the condition of the throat, ears, or lymphnodes, should be the signal for a thorough, complete physical examination.

The urine need only be examined once or twice in the first ten days of the disease. From the tenth to the fortieth day it should be examined daily, and a careful record should be kept of the quantity passed each day.

The fever does not usually require treatment. The coal tar antipyretics should be strictly avoided. A high temperature without accompanying symptoms is not dangerous, and needs no therapeutic measures. If, however, with a temperature of 104° F. or over, there is headache, restlessness, signs of discomfort, or delirium, sponge baths may be given with water at a temperature of 90° F. If the child is somnolent, a little colder water may be poured over the body at the end of the sponge bath. If the temperature is very high with accompanying symptoms, and does not respond to the sponge baths, the child may be placed in a tub of water at a temperature of 90° F., and the temperature of the water reduced to 80° F. by the gradual addition of colder water. Cold packs are often not well borne, and should only be used in the most extreme cases.

The throat requires local treatment in many cases. Older children should gargle the throat frequently with a three per cent solution of sodium borate, or a four per cent solution of borax, or a very dilute solution (one per cent) of peroxide of hydrogen. In children too young to gargle, no local treatment of the throat should be employed in the milder forms of angina. In severe angina, the throat may be syringed several times a day with one of the same solutions, unless there is severe resistance on the part of the child. When membranous angina is present, cold compresses should be applied to the throat, and changed frequently. If syringing cannot be carried out without resistance, the throat should be sprayed several times daily with a dilute solution of hydrogen peroxide. The lips should be kept soft with some simple ointment.

The lymphnodes, when enlarged and painful, should be treated by means of an ice bag, or frequently changed cold compresses. If suppuration takes place, surgical incision and drainage are necessary.

The nose should not be syringed nor sprayed, on account of the danger of the infection being carried into the Eustachian tubes. It should be kept externally clean, and the upper lip should be protected from the discharge by frequent applications of ointment.

The ears are treated as in any otitis media. During the stage of congestion, syringing with warm water should be employed. With bulging of the membrum tympani, paracentesis should be performed, but in scarlet fever the drum often ruptures spontaneously at the beginning of the process.

The scarlet fever *arthritidis* usually requires no treatment. If the pain is severe, salicylates, and hot applications may be used.

The nephritis of scarlet fever is treated in the same way as any

acute nephritis, and the treatment is described in the Division on Diseases of the Kidney.

Stimulation is required in scarlet fever, as in other acute infections, whenever there are any signs of cardiac or vaso-motor weakness, as shown by a rapid pulse. The best stimulant in such cases is caffein-sodium-benzoate. Camphor in oil given subcutaneously may be used in sudden threat of cardiac failure.

During the stage of *desquamation* the application of a simple ointment to the whole body is desirable both for the purpose of softening the disintegrated epithelium and lessening the duration of this stage, and also to prevent the spread of the contagium by means of the loosened scales.

SÉRUM THERAPY.—The treatment of scarlet fever with anti-streptococcic serum has been highly recommended by many authorities, and its value has been the subject of much discussion. It is impossible from the evidence at hand to draw any positive conclusions. This treatment was based on the theory that scarlet fever is caused by a streptococcus, which theory is now considered highly improbable. It is admitted, however, that the severe types and complications are probably caused by a secondary streptococcus infection, and this would explain the reported good results from serum therapy. Antistreptococcic serum should not be used as a routine measure. In mild and typical cases, the disease runs a favorable course anyway, and it is not advisable to run the risk of uncomfortable serum sickness. In severe cases, with membranous angina, running an unfavorable course, or in cases with severe complications, the antistreptococcic serum should be tried.

TABLE 49

Percentage of Mortality of Scarlet Fever in the Annakinderspital in Vienna from January 1, 1893, to July 1, 1904

YEAR	PER CENT	YEAR	PER CENT
1893.....	25.2	1899.....	16.4
1894.....	21.0	1900.....	12.4
1895.....	20.0	1901.....	8.9 serum
1896.....	17.6	1902.....	6.7
1897.....	11.1	1903.....	8.5
1898.....	12.3	1904 to July, 1904.....	7.6

PROBLEMS AND RESEARCH.—The one great problem in scarlet fever is that of the specific etiology. The diphtheroid bacillus of Mallory is promising, and we are now awaiting the results of its further investigation.

The following subjects in connection with scarlet fever have recently figured largely in the literature of medical research:

1. The diagnostic significance of the leukocytic inclusion bodies found in scarlet fever.

2. The streptococcus in connection with etiology.
3. The experimental transmission of scarlet fever to monkeys.
4. The value of antistreptococcic serum therapy.
5. Streptococcus vaccine therapy in the production of artificial immunity.

The inclusion bodies have been finally shown not to be characteristic.

There is still considerable difference of opinion as to the rôle of the streptococcus. A number of European authorities still believe it to be the cause of the disease. Kretschmer advances the ingenious hypothesis that scarlet fever represents an anaphylactic phenomenon due to a hypersusceptibility to the streptococcus. The arguments in favor of the streptococcus theory, and against a specific etiology, are, the varying incubation period, the occurrence of sporadic cases apparently without exposure, the good results of serum therapy, and the fact that certain observers have claimed to have found specific antibodies for the scarlet fever streptococcus, which they think differs in its biological reactions from other streptococci. Other observers, however, have failed to confirm the experimental evidence in favor of the streptococcus, and the weight of the evidence inclines toward the view that the streptococcus is a secondary invader.

There has been much difference of opinion as to whether scarlet fever has been successfully transmitted to monkeys. There have been many failures, and the reported successes have been questioned, on the ground that monkeys frequently have transient erythematous eruptions, and bran-like desquamation. It seems probable from the evidence, however, that true scarlet fever has actually been transmitted to the higher anthropoid apes, although the transmission is difficult. Lower monkeys appear to be insusceptible. This question of experimental scarlet fever is of extreme importance, as every organism which shall in the future appear as a claimant to the title of the specific cause of scarlet fever, will stand or fall by the results of animal experiment. The organism must be isolated in pure culture, and scarlet fever must be produced experimentally by inoculation with the culture, before it can be accepted as the proven cause.

The question of serum therapy has already been discussed. In a disease of which the severity, course, and fatality is so varying as in scarlet fever, it will always be extremely difficult to prove the value of any specific treatment. Serum therapy has proved unable to change or interrupt the course of typical cases.

Vaccine therapy has been employed in scarlet fever, and the usual "good results," based on utterly inconclusive evidence, have been reported in scarlet fever just as they have in every disease in which vaccine therapy has been used. There is no evidence of any value in favor of vaccines as a means of treatment. The question of vac-

cines in prophylaxis has been discussed. The evidence in their favor is mainly of the character of percentage figures in two exposed hospital wards, one with vaccine prophylaxis, the other without. Owing to the irregularities of the transmission of scarlet fever, such evidence is of no value whatever, and it will be impossible to prove the value of vaccine prophylaxis without experimental inoculation of children, or more certain experimental production of scarlet fever in animals.

MEASLES

Measles is a specific infectious disease, characterized by an exanthem, and by a characteristic affection of the mucous membrane of the mouth and respiratory tract, and of the conjunctiva. It is the commonest of all the specific infections. Measles is contagious, self-limited, and one attack usually confers an immunity which protects the individual throughout life.

ETIOLOGY. THE MICROÖRGANISM.—The organism which causes measles is, in spite of much research, still unknown. It has been demonstrated that the virus is contained in the secretions coming from the nose and mouth, and also in the blood. It has further been demonstrated that the cause of measles belongs in the class of filterable virus, as it can pass through a Berkefeld filter. These characteristics of the virus have been brought to light by the experimental production of measles in monkeys.

TRANSMISSION.—The virus of measles is an air-borne contagium. It possesses the power of floating in the air, and consequently measles is transmitted from one individual to another without direct contact. It is probable that the virus is contained in the moist particles expelled in coughing and sneezing. A susceptible child can therefore contract the disease by simply approaching a measles patient, or by entering a room in which there is a measles patient. It is consequently evident that the transmission of measles is much easier than that of scarlet fever, which requires actual contact, or an infected object to act as a carrier.

On the other hand, the virus of measles is extraordinarily short-lived outside the body. It must be transmitted directly from the patient to the exposed child. If objects are contaminated, the virus quickly dies. Consequently indirect transmission, the carrying over of the virus on contaminated objects, or by healthy carriers, is so extremely rare, that it is practically negligible. A healthy person leaving the same bed with a measles patient, and going directly into bed with another person, can carry the disease. Except for such circumstances as this, indirect transmission does not occur. There are no recorded instances of a physician carrying the measles contagium from one house to another.

THE INFECTIOUS PERIOD.—Measles is contagious from the very beginning of the prodromal stage, that is, from the very first symptom, whether that be a rise of temperature or the beginning of catarrhal symptoms. This means that *measles is contagious for three or four days before the appearance of the efflorescence*. Measles is also probably most contagious during the prodromal stage; at all events, the usual time of transmission is two or three days before the appearance of the rash. The disease is also contagious in the stage of efflorescence. The infectious period lasts usually until the fall of temperature, that is, until the time of *completion* (but not of disappearance) of the rash. As a safe outside limit, measles may be considered as no longer contagious ten days after the appearance of the efflorescence. The scales of desquamation are not infectious.

THE PORTAL OF ENTRY.—The route by which the virus of measles enters the body, is through the nose or mouth, with the inspired air.

THE INCUBATION PERIOD.—The period of incubation of measles is less variable than that of scarlet fever. It is usually ten or eleven days, sometimes nine or twelve days. The extreme limits are seven to fourteen days.

PREDISPOSITION.—Mankind is extremely susceptible to measles. Although measles is chiefly a children's disease, there is no greater susceptibility in childhood than in adult life. Few individuals are really immune, two or three per cent at most. In an epidemic in the Faroe Islands, where no measles had previously existed, 99 per cent of the population were attacked. The usual greater frequency of the disease among children is due to the fact that the majority of adults have been immunized by a previous attack, and that the conditions in childhood—school, children's parties, play-grounds—favor the transmission of the disease.

The only exception in the predisposition toward measles is seen in very young infants. Infants under six months are not very susceptible, and are rarely infected when exposed. Even in the second six months there is some immunity, as the disease does not attack so large a percentage of the exposed as later. After one year, the susceptibility becomes great.

The age at which children are most commonly attacked by measles is, in the cities at least, between two and six years. This is because the first exposure (except possibly in infancy) usually occurs at this age. Those who escape early exposure, may be attacked at any subsequent age, but most persons are attacked while still children, although some escape until adult life is reached.

IMMUNITY.—One attack of measles confers a pronounced and lasting immunity. Second attacks can occur, but they are extremely rare. Many of the reported cases of second attacks of measles are

due to the failure to distinguish between measles and rubella. Second attacks are commoner in scarlet fever than in measles.

EPIDEMIOLOGY.—As a result of the predisposition of the human race toward measles, the disease tends to occur in epidemics, which spread rapidly, soon reach their height, and quickly end, there being no more susceptible children within reach. In small and comparatively isolated localities, there may be no measles for a number of years, until one case introduces the disease, and causes a widespread epidemic. In the large towns, epidemics occur every three or four years, with freedom from measles in between. In the big cities there are always cases of measles, but widespread epidemics are not seen. There are little epidemics at times in various parts of the city.

Measles is more common in the autumn, winter, and spring than in the summer. This is probably because the schools are open at this time.

PATHOLOGICAL ANATOMY.—Beyond the morbid conditions which appear on the *skin* and on the mucous membrane of the throat, there is no especial characteristic pathology of measles. The chief lesions found post-mortem in fatal cases are those of the complications which caused death. The most common fatal complication is bronchopneumonia. Otitis media is frequently found.

In cases coming to autopsy during the stage of efflorescence, the pathological changes in the skin are clearly marked. The capillaries of the papillae are dilated and there is round cell infiltration about the walls of the vessels, about the sweat and sebaceous glands, and about the hair follicles.

The mucous membrane of the respiratory tract shows a catarrhal inflammation, which has no peculiarities characteristic of measles.

SYMPTOMS. PRODROMAL STAGE.—This is the period between the beginning of the symptoms and the first appearance of the efflorescence on the skin. The length of the prodromal stage varies from one to five days. In the great majority of cases it is two or three days, sometimes four days, rarely one or five days.

The invasion is characterized by severe catarrhal conditions affecting the nose (coryza), the eyes (lachrymation), and the throat and upper-air passages (cough). In the first twenty-four hours the temperature rises to 101° or 102° F., and often to 104° F. The height of the temperature on the first evening is a fair indication as to the severity of the coming disease. Thus a temperature of 105° F. indicates a severe case. An important point to be noticed regarding the prodromal symptoms is that after the first twenty-four hours there is in a large number of cases a remission in the temperature, which goes down, perhaps to 99.5° or 98.6° F. and remains down for about twenty-four hours, when it again rises. The *cough*, *coryza*, and *lachry-*

mation, which appear early in the prodromal stage, do not abate, but rather increase, during this remission of the temperature. This is an important point to remember, as the child who seems quite sick and loses its appetite while the temperature is high during the invasion of the disease, seems brighter and has a return of appetite on the second day when the temperature is lower. This peculiarity of the prodromal stage is often misleading both to the parents and to the physician, who, because the child appears so much better, are led to believe that one of the infectious diseases is not developing. In infants and young children, the prodromal stage may begin with a convulsion, but this is unusual, and if it occurs it is not, as a rule, particularly severe, and does not necessarily make the prognosis more grave. Headache in the prodromal stage is quite frequent; vomiting is rather rare. The tongue is usually furred, and the mucous membrane of the throat shows at first only the appearance of an ordinary catarrhal inflammation. The cough is dry, and often severe and racking, and sometimes hoarse and ringing, showing the involvement of the larynx. The nose begins to run. The conjunctiva is red and swollen, as is the caruncle at the inner angle of the eye. The discharge from the eyes is usually watery, sometimes purulent.

The whole picture during the prodromal stage resembles that of a severe catarrhal cold, or an attack of grippe, and there is nothing to show that it represents the beginning of measles, until the appearance of Koplik's spots, or of the measles efflorescence on the mucous membrane of the mouth. These signs are often overlooked, so that the true diagnosis is not suspected until the appearance of the efflorescence upon the skin.

KOPLIK'S SPOTS.—If the mucous membrane of the mouth be carefully and systematically examined during the prodromal stage, it is often possible to make a positive diagnosis of measles two or three days before the appearance of the efflorescence. This is based on the finding of Koplik's spots, which are pathognomonic of measles. They appear on the mucous membrane lining the cheeks, usually near the molar teeth, and consist of light red spots about the size of the head of a pin, in the center of which are minute white or bluish-white points, no larger than the finest grains of sand. The white points consist of fatty degenerated epithelium and detritus. In many cases there is so much catarrhal reddening of the mucous membrane of the mouth, that the light red spots do not stand out clearly, or else, especially in anemic children, there is no reddened base, and only the minute white points are seen.

The number of Koplik's spots is very variable. Sometimes there are only two or three, and the white points are so small, that they are found with the greatest difficulty. They can only be satisfac-

PLATE IX.

FIG. 1.

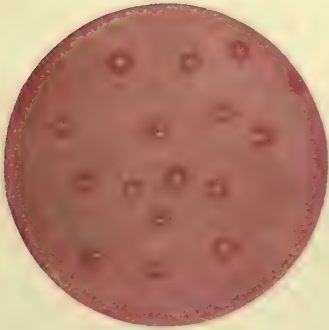


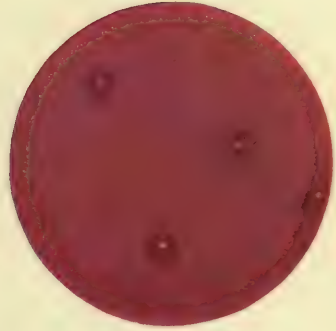
FIG. 2.



FIG. 3.



FIG. 4.



THE PATHOGNOMONIC SIGN OF MEASLES (KOPLIK'S SPOTS)

FIG. 1.—The discrete measles spots on the buccal or labial mucous membrane, showing the isolated rose-red spot, with the minute bluish-white centre, on the normally colored mucous membrane.

FIG. 2.—Shows the partially diffuse eruption on the mucous membrane of the cheeks and lips; patches of pale pink interspersed among rose-red patches, the latter showing numerous pale bluish-white spots.

FIG. 3.—The appearance of the buccal or labial mucous membrane when the measles spots completely coalesce and give a diffuse redness, with the myriads of bluish-white specks. The exanthema on the skin is at this time generally fully developed.

FIG. 4.—Aphthous stomatitis apt to be mistaken for measles spots. Mucous membrane normal in line. Minute yellow points are surrounded by a red area. Always discrete.—*Med. News*, June 3, 1899.

torily seen by daylight, and require a strong light, good eyes, and close observation. The child should be held close to a window, in the position used for the examination of the throat, and a spatula or handle of a teaspoon should be inserted at the corner of the mouth, and the cheek retracted from the teeth. At other times the spots are very clear and numerous, covering thickly the lining of the cheek, and often extending onto the mucous membrane of the lower lip. Their number increases up to the time of the appearance of the skin eruption, and they rapidly disappear on the first or second day of the stage of the efflorescence.

Koplik's spots appear at a variable time before the efflorescence on the skin, *most commonly two days before*. They may in rare cases appear as long as four days before the rash, while sometimes they do not appear until simultaneously with the rash. They may not be seen at all in very young or atrophied infants.

Koplik's spots are a sign of extreme importance in the diagnosis of measles. When present, they are diagnostic, as they are seen in no other disease. The difficulty lies in the diagnosis of the Koplik's spots themselves. They are easily distinguished from thrush, and are much smaller than the lesions of aphthous stomatitis.

THE ERUPTION IN THE MOUTH.—The rash of measles begins on the mucous membrane of the mouth toward the end of the prodromal stage. This is to be distinguished from the Koplik's spots. The eruption in the mouth is in every way similar to the later eruption on the skin. It appears one or two days before the efflorescence on the skin, usually later than the first appearance of the Koplik's spots. These lesions, which are especially pronounced on the soft and the hard palate, are represented by papules or macules of a dark red and later purplish-red color, of different sizes, and considerably larger than the punctate macules which were described in connection with the throat in scarlet fever. These papules in certain cases are arranged crescentically, and may sometimes be found to have coalesced in some parts of the fauces. The mucous membrane between the lesions is comparatively normal in color, although there may be a slight hyperemia of the entire throat. This hyperemia, however, is not nearly so intense as is seen in the throat in scarlet fever. The exanthem in the throat is at its maximum with the beginning of the cutaneous efflorescence, and may take as long as three or four days to disappear. It is often not clear and characteristic, and is not so important in the early diagnosis of measles as are the Koplik's spots.

END OF THE PRODROMAL STAGE.—After the peculiar remission of the fever, which most commonly occurs on the second day of the disease, the temperature rises again, and remains high, or continues

to creep higher, during the remainder of the prodromal stage. The discomfort and constitutional disturbance accompanying the fever, and the catarrhal symptoms, remain severe, or increase in severity. On the day before the appearance of the efflorescence, all the symptoms reach their maximum severity.

THE EFFLORESCENCE.—The physician who is watching the development of a case of measles, now looks for the first appearance of the rash, which begins as little red spots, which usually first appear behind and in front of the ears, on the face, or on the neck. From these situations the efflorescence spreads rapidly, first to the back, then over the entire trunk, then to the upper arms, then to the thighs, and finally to the forearms and legs, so that the entire body becomes covered. It usually takes two days for the entire body to become involved, and another day for the rash to reach its greatest intensity. At this time, however, the rash has already begun to fade on the parts of the body where it first appeared, so that for the rash to reach its greatest intensity in any part, and then begin to fade, takes about two days. The rash fades in the order of its appearance.

The single spot of measles begins as a tiny macule, which increases in size. As the spot grows, a prominence forms in the middle, which becomes palpable as a slightly raised papule, and corresponds to a gland or hair follicle. The spot quickly becomes of a size varying from a pin-head to a pea, and as it grows it becomes irregular in outline. The fully developed spot is slightly but entirely raised above the level of the surrounding normal skin.

The color of the spots is at first light red, but as the papules develop, the color becomes a bright, fiery red.

In the beginning, when the spots are small, they are sparsely scattered, but as they grow larger, new spots keep coming in between. In certain parts of the body, particularly on the face and back, the rash becomes confluent, forming large red areas, with only small islands of normal skin.

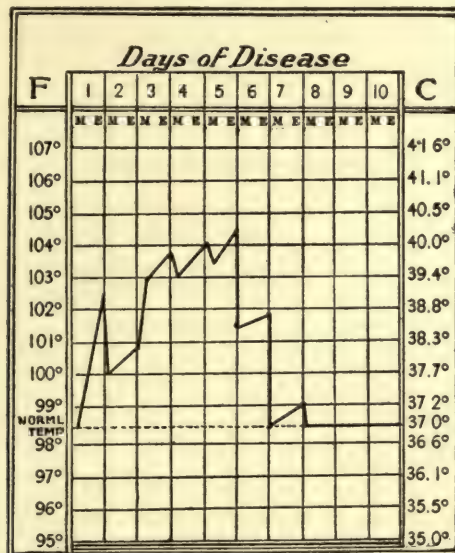
The fading of the rash is rapid, lasting about two days, so that the entire period of the exanthem is from four to five days. Until the rash begins to fade, the color disappears entirely on pressure, but after fading has begun, a certain amount of color remains on pressure, as some blood pigment has escaped from the vessels. This brownish pigmentation becomes more conspicuous after the rash fades, especially in full-blooded children, and may remain visible for from ten to twenty days.

DESQUAMATION.—A light desquamation begins with the disappearance of the efflorescence. The desquamation is usually furfuraeous in character, that is, the epithelium is cast off in fine flakes, and is thus distinguished from the large lamellar flakes occurring during

the period of desquamation in scarlet fever. The desquamation begins in the order in which the efflorescence came out, namely, first on the face and later on the chest. The furfuraceous character of the desquamation is especially noticeable on the sides of the nose. The desquamation on the body is so slight and fine as to be hardly noticeable. Older children sometimes complain of itching, especially of the legs, during the stage of desquamation.

THE TEMPERATURE CURVE.—In typical cases of measles, the temperature curve is often quite characteristic. The peculiar fall of temperature on the second day of the prodromal stage, one or two days before the appearance of the efflorescence, has already been

CHART 9



Typical measles

mentioned. The temperature reaches its maximum on the second day of the efflorescence, remains high another day until the full development of the eruption, and then falls abruptly by a sharp or broken crisis. If the temperature fails to fall before the fourth or fifth day after the appearance of the exanthem, it is strongly suspicious of a complication. The highest point reached by the fever is usually at least 103° F., and may be as high as 105° F. Deviations from the typical temperature curve are common in cases otherwise typical, especially a fall of temperature by lysis beginning at the height of the exanthem.

ACCOMPANYING SYMPTOMS.—The general condition is much affected both in the stages of invasion and of efflorescence. Severe cough, headache, and photophobia are the most troublesome symptoms.

Delirium, especially at night, is often present. The appetite is almost entirely lost.

The conjunctivitis increases in the stage of efflorescence. The secretion may become purulent, and the eyelids are often stuck together in the morning. The rhinitis also increases, and the swollen mucous membrane and purulent secretion often render breathing difficult.

The tongue is dry, and heavily coated. The throat is somewhat reddened, and the exanthem may still be visible on the mucous membrane after its appearance on the skin.

The cough often improves with the beginning of the eruption, as does the laryngitis.

The lungs in the majority of typical cases are normal to auscultation and percussion. Often, however, medium and coarse moist râles are heard.

The heart and circulatory apparatus show little evidence of special disturbance. The pulse is rapid, corresponding to the fever, and in young children may reach 160 to 180 without becoming poor in quality.

The urine in mild cases is concentrated, and slightly diminished in quantity. With high fever there is usually a small amount of albumin, and a few casts and red blood corpuscles. A true nephritis is very rare. During the stage of efflorescence the diazo reaction is present.

During the period of efflorescence, when the temperature is still raised and the eruption is at its maximum, it is usual to have, in addition to the symptoms of cough, coryza, and lachrymation, a slight disturbance of the intestines, represented by small, frequent, loose discharges, apparently arising from irritation of the rectum and descending colon. This condition is seldom a serious one, and no especial attention need be paid to it unless it should continue for some days, or after the maximum of the temperature and efflorescence has been passed for a day or two.

The lymphnodes are slightly enlarged. The spleen is not palpable.

THE BLOOD.—The blood picture in measles is very characteristic, and recent researches have shown that the changes begin during the stage of incubation, so that a change in the blood finding is really the first symptom of the disease. In the blood of normal children the lymphocytes predominate over the neutrophils. During the stage of incubation there begins a relative decrease in lymphocytes, and increase in neutrophils, which begins on the average six or seven days before the eruption. This is caused by a diminution in the absolute number of lymphocytes, which becomes marked enough to cause an actual *leukopenia*, which may appear anywhere from eight

days before the eruption to simultaneously with the rash, but is seen on the average four and one-half days before. The neutrophiles come to predominate in the differential count, and this displacement of the blood picture appears on the average four days before the beginning of the rash. The eosinophiles diminish during the incubation period, and are absent during the stage of efflorescence. The white count reaches its lowest point at the height of the exanthem. With the fall of temperature, the lymphocytes increase, the eosinophiles reappear, and the polynuclear neutrophiles may, after deferrescence, be relatively below the normal.

These changes are considered by many writers of the highest importance in the early recognition of measles, as they usually occur several days before the appearance of Koplik's spots. If they were as constant and typical as described, it would be possible by a daily examination of the blood of a child who had been exposed to measles, to recognize the approach of the disease during the stage of incubation, and this would be very useful in prophylaxis, especially in hospitals. It is often possible to make an early diagnosis of measles in this way, but I have not found the changes as constant and typical as described.

The most useful feature of the blood examination in measles is the leukopenia. A leukocytosis always points toward a complication.

CONVALESCENCE.—With the fall in the temperature, all the symptoms disappear rapidly. In one or two days the child feels well. The cough lessens, and ceases in a few days. The conjunctivitis and rhinitis clear up more slowly, but usually a week after the appearance of the efflorescence the child is fully convalescent, and by another week or ten days is well, the only trace of the disease being the slight pigmentation of the skin.

VARIATIONS IN TYPE OF MEASLES.—Measles during epidemics and in sporadic cases varies much in its type, and presents great differences in its prodromal stage, in its dermal lesions, in its desquamation, and in its entire course. Through a lack of appreciation of this fact, the diagnosis of other diseases, such as rubella and various forms of erythema, is continually being made, when, in fact, the disease represents one of the more unusual forms of measles. If these variations in measles were better understood, we should not find the disease rubella so often diagnosed.

At times, the duration of the stage of incubation of measles varies considerably. Instead of the usual prodromal stage, certain cases during epidemics of undoubted measles show few, if any, prodromal symptoms.

In addition to the usual catarrhal symptoms, in some cases there are vomiting and sore throat. Again, instead of a considerable ele-

vation, the temperature may be scarcely above the normal degree. Epistaxis of a mild form is sometimes met with.

The efflorescence, which in typical cases usually consists of papules, may vary so as to simulate closely a common erythema, constituting the form called *laevis*, or may closely simulate a papular erythema. Again, the efflorescence may in certain cases be represented by minute vesicles or milia, characterizing the form called *miliarius*. Any of these forms may be confluent, but, as a rule, only upon the face.

There is another form of efflorescence which occurs in measles, which is rare, and of a more serious nature than the common benign forms which are met with ordinarily. This is called the *hemorrhagic* or *malignant* form, and is represented on the skin by small capillary hemorrhages. It is often rapidly fatal, and at times appears to be part of a general hemorrhagic diathesis or symptomatic purpura, characterized by epistaxis, hematuria, and hemorrhages from other localities. The temperature in these cases is not typical, as it does not remit in the prodromal stage, thus depriving us of an important means of diagnosis; but a doubt as to the nature of the disease does not last long, as the other symptoms soon become prominent. The more prolonged the course of this form, the better the prognosis, for if fatal it is usually quickly so. It may be complicated by a malignant bronchopneumonia.

The efflorescence, besides differing in its form, may vary to a great degree in its intensity. Thus, we may have every grade of papule or macule, from the smallest to the largest, and varying from a dark purplish to a light pink color. In like manner, although the arrangement of the efflorescence, especially on the chest, is somewhat crescentic, yet during epidemics of undoubted measles this crescentic shape is often absent. Instead of the efflorescence first appearing on the face and then extending to the thorax and extremities, we may find in undoubted measles that it begins first on the chest or some other part of the body; or the efflorescence may appear on the face and thorax simultaneously. We may also find that in certain cases the efflorescence appears first on the abdomen, or on the thighs, and yet the presence of other typical and undoubted cases of measles in the vicinity or in the same house assures us that we are dealing with the same disease. The efflorescence, instead of lasting for a number of days, may be evanescent, and may subside within twenty-four hours.

The desquamation of measles is of so light a grade that it is not surprising that in some cases no desquamation whatever is detected. Cases in which desquamation occurs without efflorescence are highly improbable, although such have been reported.

During certain epidemics of undoubted measles, cases have not

infrequently been noted in which the post-aural and cervical glands were markedly enlarged.

There is a form of measles, called the *recurrent*, which simulates relapsing fever. The main characteristic of this form is the high fever. The temperature will sometimes be raised for five or six days, will then become normal for seven or eight days, and will then rise again with a recurrence of the symptoms. This is a very unusual form, and one which needs merely to be mentioned here. It is accompanied by the general symptoms connected with the nose, eyes, and bronchi which are met with in the typical form of measles.

Relapses occur in measles, but they are uncommon.

In reviewing the pictures which have been given of these variations, it must be evident that, although in the large proportion of cases measles runs so typical a course that the diagnosis is very easily made, yet such great variations in type are always so liable to occur that we should be extremely careful not to make a diagnosis of certain other diseases, such as rubella, except under unusual circumstances. This is important, because we know that during epidemics of well-marked measles all these great variations as to incubation, prodromata, efflorescence, desquamation, and the entire course not infrequently arise.

COMPLICATIONS AND SEQUELAE.—There are quite a number of complications and sequelae which may occur in the course of measles. The most common of the serious ones are *pneumonia*, and *tuberculosis*.

BRONCHOPNEUMONIA.—The bronchitis which is so common an accompaniment of measles sometimes appears in a more severe form, attacking the smaller bronchi as well as those of medium size, and may result in a bronchopneumonia, which is much more common as a complication of measles than is lobar pneumonia. The bronchopneumonia does not, however, appear to be more severe when it arises as a complication of measles than when it occurs separately from that disease. Bronchopneumonia as a complication of measles may occur very early in the course of the disease, even during the stage of invasion; but it occurs most commonly towards the end of the second week.

When, therefore, after the efflorescence has faded and the fever has subsided, the temperature again rises without evidence of local inflammation in the throat, ears, or glands, we should suspect that a bronchopneumonia is developing. The additional symptoms of quickened respiration and movement of the alae nasi will render still more probable the supposition that this complication is arising, even though no consolidation is detected in the lung itself.

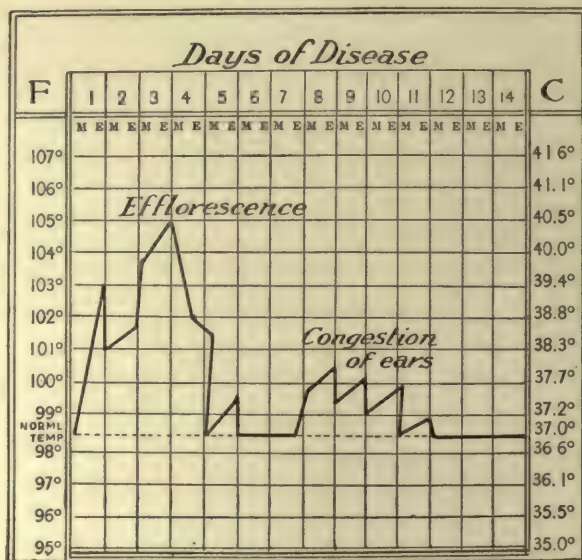
The congestion of the larger bronchi, which appears to be almost

a part of the measles, may become subacute and chronic, instead of, as is usually the case, passing off soon after the maximum of the temperature and efflorescence.

Pleuritis may occur in the course of measles, but is not so common as pneumonia.

OTITIS MEDIA.—This is a common complication of measles. It shows no special characteristics differing from the otitis media occurring as a complication of other acute infectious diseases.

CHART 10



Measles with congestion of membranae tympanorum during stage of efflorescence

EYE.—In addition to the conjunctivitis which is a common accompaniment of measles, and which, as a rule, requires no treatment beyond the protection of the eyes from light, the inflammatory process may extend to the deeper tissues of the eye and cause other grave lesions, such as *blennorrhagic conjunctivitis*, *keratitis*, and *iritis*. These complications should be treated at once by a skilled ophthalmologist.

THYROID GLAND.—In a very few cases an acute swelling of the thyroid gland may take place during the course of measles. This swelling of the thyroid gland may even cause marked dyspnea by pressure, but it usually disappears in two or three days. In some cases, however, a formation of pus has taken place, followed by destruction of a part of the gland. In intractable cases of this kind it has been found that the external application of iodine is useful.

LYMPHNODES.—Enlarged cervical lymphnodes are not so common

in measles as in scarlet fever, but they may occur, and may even prove serious from the occurrence of suppuration.

TUBERCULOSIS.—The most common sequela of measles is tuberculosis. This means that in a child already infected with tuberculosis in the primary stage, measles markedly predisposes toward the development of secondary manifestations. These may take the form of general miliary tuberculosis, or secondary tuberculosis of some organ or part of the body. Tubercular disease of the joints seems to show a special liability to follow attacks of measles. It is noticeable that when a patient with a tubercular joint has an attack of measles, the process in the joint is apt to become temporarily more active, and the prognosis is comparatively more grave. The organ which in measles is most commonly affected by tuberculosis is the lung, and the most common form of tuberculosis of the lung is a tubercular bronchopneumonia.

PARALYSIS.—Another sequela, although a rare one, is paralysis. Cases thus complicated have shown mostly a paraplegia, and, according to Osler, frequently can be classified as post-febrile polyneuritis, although it is possible that some of them may be due to a rapidly ascending myelitis.

NOMA.—A very rare sequela of measles is the disease noma (*can-
crum oris*).

Among the rarer complications of measles are *empyema*, *endocarditis*, *pericarditis*, and *membranous laryngitis*. *Catarrhal laryngitis* and *tracheitis* are not infrequent accompaniments of the acute stage of measles. Edema of the glottis is rare, but has been known to occur.

The irritation of the intestine, occurring commonly during the height of the efflorescence and temperature, sometimes becomes much more severe from the development of *colitis* as a complication.

DIAGNOSIS.—In order to understand how difficult it sometimes is to diagnose measles, we must recognize that it is one of the most variable diseases with which we have to deal. During epidemics of undoubted measles, cases arise which differ materially from the disease as it appears in its typical form, yet these cases, by producing the typical form in other individuals, prove that they are all caused by the same contagium. In like manner, certain epidemics may be characterized by irregular forms of the disease, and, as true measles can rarely occur more than once in the same individual, the recognition of a sporadic case is often difficult. As in other diseases of the skin, we should recognize measles not by any particular dermal lesion, but by the peculiarities of the prodromal symptoms, the general course and location of the efflorescence, the time of the maximum of the efflorescence, and the character of the desquamation.

Thus, a prodromal stage of three or four days, characterized by catarrhal symptoms of the eyes, nose, and upper air-passages, by the presence of Koplik's spots in a large majority of cases, and a papular efflorescence appearing first on the face, differentiates the disease from the various conditions for which it might be mistaken.

During the prodromal stage, a positive diagnosis depends usually upon the finding of Koplik's spots. Until these appear, the diagnosis must always be in doubt. The next diagnostic sign to develop is the eruption in the mouth, and ultimately the diagnosis rests on the recognition of the character of the eruption on the skin.

When the exanthem of measles is markedly papular, one might think of the possibility of *variola*. After one or two days, however, the typical vesicular character of the smallpox eruption develops. Furthermore, in *variola* the temperature falls with the appearance of the eruption, while in measles it rises.

A very markedly confluent rash in measles might suggest *scarlet fever*, but there are always parts of the body where the measles rash is discrete, and these bear no resemblance to scarlet fever. In scarlet fever the absence of catarrhal symptoms, of Koplik's spots, and of a long prodromal stage, and the presence of angina, strawberry tongue and leukocytosis, makes the differentiation usually easy.

The efflorescence of *rubella* is similar to that of measles, but is usually paler, more sparsely scattered, and the spots are smaller. The absence of prodromal symptoms, Koplik's spots, high fever, and marked constitutional disturbance, is the characteristic feature of *rubella*.

In various infections, and also in certain toxemias not due to infection, such as serum sickness, or after the taking of certain drugs, a *toxic erythema* may appear on the skin, which may resemble the efflorescence of measles. In most of these cases, however, the rash is polymorphous or changing in character, there are areas where it does not resemble measles, and it is usually not distributed all over the body. The catarrhal symptoms, Koplik's spots, and blood findings of measles are absent.

In rare cases the *syphilitic roseola* has been mistaken for measles, in spite of the absence of the other characteristic symptoms. I have even seen a case of *typhoid fever* with a very profuse crop of rose spots, diagnosed as measles.

PROGNOSIS.—The prognosis of measles is good. The disease lacks the uncertainties of scarlet fever, and most children recover completely. The only dangers are from the development of bronchopneumonia, or of one of the fatal secondary forms of tuberculosis. Both of these dangerous complications appear most often in infants or very young children. In children over three years of age, they

are comparatively rare. Bronchopneumonia is seen most often in feeble or rachitic infants. In such cases, when the disease begins with a severe bronchitis, and when the eruption is not well marked, the prognosis is very uncertain.

PROPHYLAXIS.—It is often said that as every individual must have measles, it is useless to attempt to protect healthy children, and that it is best to allow them to become exposed while well, in order to protect them from acquiring the disease at some future time, when they may be in poor health, or when measles may be more inconvenient. I do not at all agree as to the desirability of such a plan. One can never be sure, no matter how well a child seems, that the disease will run a mild course, and if a complication does develop, the physician who is responsible for the health of the child will have much to reproach himself for. It must also be remembered that measles is mainly dangerous in young children. It is consequently especially important to protect the very young, or the weak and sickly. It is not true that measles runs a more severe course in adults.

Whenever a child becomes sick with any symptoms compatible with measles, it should be rigidly isolated. If this is done, there is a possibility that the other children in the household may escape, especially the younger ones. If the diagnosis of measles is confirmed, the isolation should be continued, the patient and its nurse being treated in the same way as in scarlet fever, except that rigid isolation of the nurse is not necessary. She may go in and out, but it is better for her to be kept away from the other children.

The rigid disinfection of all clothing and other articles used in the sick room, which is practiced in scarlet fever and diphtheria, is not necessary in measles. On the other hand, other children should not be allowed near the sick room. Whenever possible, in private practice, I send them out of the house.

When measles occurs in kindergartens, day nurseries, or any place where *young* children congregate, the institutions should be closed. It is not, however, necessary to close the common day schools on account of measles, as epidemics cannot be checked in this way. In children's hospitals, the ward in which measles occurs should admit no new patient until fourteen days after the appearance of the last case.

The measles patient should be kept in isolation until fully convalescent, usually two weeks at least. After release, disinfection of the sick room is unnecessary. It should simply be given a good airing.

TREATMENT.—The treatment of measles is essentially symptomatic. There is no known means of producing immunity to the

disease or of shortening its course. It is a self-limited disease, and the treatment should be directed towards the protection of the organs which are most likely to be attacked by complications. Bearing in mind that the eyes, the nose, and the throat are affected in the prodromal stage, that later the skin is in a very sensitive condition, and that the lung is frequently the seat of some complication, we should direct our treatment especially to the care of these organs.

The child should be placed in a room kept at an equable temperature, 68° to 70° F., and well ventilated. The room should be darkened, and the eyes should be protected from light during the whole course of the disease. Unless this precaution is taken, the eyes are often seriously affected for many months after the measles itself has disappeared. The child should be kept in bed until the temperature has been normal for a few days, the efflorescence has faded entirely, and the desquamation has almost ceased.

The diet during the period of the high temperature should be soup, milk, and bread. Later, when the temperature is normal and desquamation has begun, the child can gradually have its diet increased, until by the third week from the beginning of the attack it is having its usual food.

The cough, though very troublesome at times, does not, as a rule, require any special treatment, as it will in most cases pass off of itself in a few days. While it continues, it can be treated with some simple medication, such as camphorated tincture of opium in cold water in doses of 5 to 10 minims.

For the irritation of the nose, some simple refined oil, such as oleum petrolatum album dropped into the nose with a medicine-dropper is useful. Atomization should be avoided because of the danger of starting an acute inflammation of the middle ear through the Eustachian tubes. During the invasion of the disease, however, these catarrhal symptoms are exceedingly difficult to control by any treatment whatever.

As at times there is great irritation of the skin during the period of efflorescence, a powder should be applied thickly to the entire body and limbs. In place of the powder, some simple ointment such as petrolatum, may prove to be more soothing.

As a rule, the child should be kept in an equable temperature for at least three weeks, and at the end of that time, if the desquamation has ceased, it may be allowed to go out of its room, and out of the house a few days later in pleasant weather. For several months, however, it should be carefully protected from sudden changes of atmosphere, as the catarrh of the air-passages is so likely to leave them in an extremely sensitive condition that a very slight irritation may cause a recurrence.

PROBLEMS AND RESEARCH.—The central problem in measles is that of the etiology. Every effort to discover the specific micro-organism which undoubtedly causes the disease, has failed. The results of blood cultures have been uniformly negative.

The most significant step in advance taken by research workers on measles, has been the successful transmission of the disease to monkeys, by inoculating their noses and throats with the secretions of a measles patient. Through this means it has been discovered that the virus is present in these secretions as well as in the blood. It has further been demonstrated that the virus can pass through a Berkefeld filter, and that the infectivity of the virus diminishes as defervescence is approached, and disappears in convalescence. It has further been demonstrated that the products of desquamation are not infectious.

This production of experimental measles opens the way to much further study of many characteristics of the virus. It is possible that these researches will eventually be crowned by the same brilliant result as in poliomyelitis, and that a way will be found to cultivate the virus artificially.

The order of appearance of the rash bears a connection with certain characteristics of the blood supply. It has been suggested that the virus may agglutinate in the capillaries.

Herrman, taking advantage of the immunity of infants, has tried protective inoculations in infants under five months. The results are promising but not conclusive.

RUBELLA

(German Measles; Rötheln)

Rubella, or German measles, is a specific infectious disease characterized by an efflorescence resembling measles but of milder grade, and by the absence of catarrhal symptoms, high fever, and marked constitutional disturbance. The disease is contagious, and occurs chiefly in epidemics.

There has been in the past considerable doubt as to whether the clinical picture of rubella represents a disease *sui generis*. Many authorities believe it to represent a mild and atypical form of measles. This doubt as to the separate identity of rubella could not possibly exist in the mind of anyone who had ever seen an epidemic. The evidence in favor of the separate existence of rubella lies in the fact that in epidemics, the clinical picture in children who contract the disease by known exposure always retains its particular characteristics, and never resembles typical measles. Furthermore, the statistical evidence of most epidemics has shown that rubella actually is

seen more often in children who have already had measles, than in children who have not.

ETIOLOGY. THE MICROÖRGANISM.—The organism causing rubella has not been discovered. Practically nothing is known of the characteristics of the virus.

TRANSMISSION.—Rubella is transmitted from one individual to another in much the same way as measles. The contagium is only exceptionally carried by a healthy person, or on objects. The virus is short-lived outside the body.

Sporadic cases are rare. The disease occurs chiefly in local epidemics, which do not affect a large percentage of the population. Epidemics occur at rather long irregular intervals, which may amount to many years. They are seen most often in the spring, and usually last several months.

The disease is contagious from the time of the first symptom, the infectivity reaching its height at the time of the exanthem, and ceasing with its disappearance. The portal of entry is unknown.

PREDISPOSITION.—The susceptibility to rubella is much less than to measles. When an epidemic occurs in a children's institution so that all are exposed, about half contract the disease. Outside of such institutions the incidence is much less.

The most susceptible are children from three to twelve years of age, especially school children. Whether this is due to a special susceptibility in childhood, or to the fact that the conditions of life in childhood favor the spreading of any contagious disease, is not known. Older infants are frequently infected, and the disease is fairly common in young adults. Immunity to measles gained by a previous attack does not protect against rubella. More than one attack is rare.

INCUBATION.—The stage of incubation in German measles is long, from *seventeen to twenty-one days*. Rarely is it as short as fourteen days.

SYMPTOMS. PRODROMAL STAGE.—In the majority of cases there are no prodromal symptoms in rubella, the first thing to attract attention being the efflorescence. Sometimes for from *half to one day* before the appearance of the rash there is malaise, fretfulness, slight sore throat, slight fever, and the symptoms of a mild cold in the head. These symptoms are not severe enough to be especially noted, and do not suggest a severe process of any kind, and the physician usually first learns of them through his inquiries made after the appearance of the rash.

THE EFFLORESCENCE.—The exanthem of rubella appears first on the face, or about the ears, and spreads very rapidly, so that usually

in half a day the skin of the entire body is involved. The spots at first are about the size of the head of a small pin, and grow somewhat larger, but do not reach the size of the measles papules. As compared with measles the spots are not only somewhat smaller, but also paler, not so much raised above the normal surface, and more regular in outline. Their shape is round or oval. In further contradistinction to the rash of measles, that of rubella is more uniform in the size of the papules, more sparsely distributed, more evenly distributed, and does not become confluent, except sometimes on the cheeks. In the beginning the entire face sometimes seems reddened.

The rash is often so much paler than that of measles, that it may be overlooked entirely. The color disappears on pressure, except that when fading it leaves behind a slight pigmentation which is less than that of measles.

The efflorescence of rubella is usually most marked on the face, back, and extensor surfaces of the extremities, or on parts of the body where the clothing presses. It is seldom seen at its fullest development all over the body at the same time, so that on the face it is already fading when the body is involved, and is fading on the body when it reaches the limbs. Often large areas of the body remain uninvolved.

The rash remains visible in any one place from one to two days, and the whole period of efflorescence is usually from two to three days.

At times the efflorescence is composed of such small papules, that it resembles scarlet fever (scarlatiniform type). According to some observers this type is never seen on all parts of the body in epidemics of rubella, but only on certain parts such as the chest and thighs. According to other observers a general scarlatiniform type has been seen in rubella epidemics. The former authorities believe a general scarlatiniform rash means not rubella, but Dukes' disease ("fourth disease"). The latter authorities do not believe in the separate identity of Dukes' disease. Occasionally the rash of rubella shows urticaria-like lesions.

No desquamation is observed in the majority of cases, but at times there is a very fine, powdery desquamation.

OTHER SYMPTOMS.—The most important symptom of rubella beside the efflorescence, is an *enlargement of the peripheral lymph-nodes*. This is a constant symptom of German measles, and may occur from two to four days before the appearance of the exanthem. The lymphnodes most markedly involved are those of the neck, especially the post-auricular group. The glands reach a size varying from that of a bean to that of a hazel nut, and are often tender to pressure. The swelling does not disappear for one or two

weeks. The axillary and inguinal lymphnodes are also involved. Cases have been described of rubella without exanthem, but with lymphnode enlargement, occurring during epidemics.

The mucous membranes are slightly if at all affected. At most are seen slight redness of the conjunctivae, slight rhinitis, slight reddening of the tonsils and pharynx, and slight enlargement of the lymph follicles. Forchheimer has described an eruption in the mouth as an enanthem which he believes is characteristic of German measles, and states that it is very short-lived, fading away within the first twenty-four hours, and is localized upon the velum of the palate and on the uvula, but rarely invades the hard palate or any other part of the mouth. The efflorescence consists of macular, distinctly pink-red spots resembling the roseola of typhoid fever, arranged irregularly, not crescentically, about the size of large pin-heads, very little elevated above the level of the mucous membrane, and with very little infiltration. Koplik's spots are never seen in rubella.

There is often a brief and moderate elevation of temperature in the prodromal stage. The fever may go to 101° F., 102° F., and rarely to 103° F., on the first day of the efflorescence. It quickly falls, even while the eruption is still spreading. Many cases run their entire course without fever.

The general condition is usually little disturbed. Often the children do not feel sick at all. The first case in a family is seen by the physician usually only through fear of measles or scarlet fever, and the parents often do not seek medical care for later cases.

Only very exceptionally are there any severe symptoms, such as severe angina, or bronchitis. Complications are practically never seen.

The blood shows no characteristic changes.

DIAGNOSIS.—In sporadic cases the diagnosis of rubella is often difficult; in epidemics it is comparatively easy. The diagnosis, as in all the exanthemata, cannot be based on the efflorescence alone, but the entire clinical picture must be taken into consideration.

Measles presents the most difficulty. If the case is observed daily from the beginning of the symptoms, Koplik's spots should be observed at some time in measles. Their presence excludes rubella; their absence is in favor of rubella, but is not positive, as they may be very few, and are easily overlooked. The second point of most importance in the differential diagnosis, is whether or not the child has already had measles. A foregoing measles speaks strongly for rubella. The rash in measles is more marked, redder, more raised, more diffuse, and presents a much more imposing picture. It is in mild cases of measles with atypical efflorescence that the most difficulty in diagnosis is encountered. Notable conjunctivitis, catarrhal

affection of the upper air-passages, and high fever, favor measles. The absence of a prodromal stage and the presence of enlargement of the cervical lymphnodes favor rubella. The long incubation period of rubella, at least fourteen days, is sometimes a help in diagnosis. The diazo reaction in the urine is said to be absent in rubella, while it is present in measles. The blood examination is not of much assistance, as neither disease is accompanied by a leukocytosis.

Scarlet fever rarely comes into consideration in differential diagnosis. The cases of rubella with a scarlatiniform rash usually show some areas where the appearance of the rash is incompatible with scarlet fever. The mildness of the constitutional disturbance, and the absence of marked angina and strawberry tongue, exclude scarlet fever.

Some of the *toxic erythemata* with a measles-like rash, present considerable difficulty at times in differential diagnosis. The rash is usually less uniform, but the diagnosis can only be made by taking all the circumstances into consideration.

PROGNOSIS.—The prognosis is good. Rubella is the mildest and most favorable of all the specific infectious diseases.

PROPHYLAXIS.—Special measures of prophylaxis are unnecessary. Isolation should be enforced only when there is any doubt of the diagnosis, while the physician is waiting to decide between measles and rubella.

TREATMENT.—No special treatment is required. If there is any fever or constitutional disturbance, the child should be kept in bed, with a light diet, the treatment being that of a mild case of measles. Children should be kept out of school for a week or ten days, but when the temperature is normal and there are no symptoms, may go out doors.

PROBLEMS AND RESEARCH.—The chief problem in rubella is that of the etiology. Very little research work has as yet been devoted to the disease. Physicians have been engaged in the more exact description of the clinical features.

DUKES' DISEASE

(“Fourth Disease”)

In 1900 the English physician Dukes described as a new contagious disease a condition which resembled mild cases of scarlet fever, but which did not appear to be either scarlet fever, measles, or rubella, and which he consequently designated as “the fourth disease.”

Dukes observed several epidemics, and described the disease as follows: There are usually no prodromal symptoms, at most slight

malaise and sore throat. In a few hours the body becomes thickly covered with a pale, punctiform efflorescence. There is some red-dening of the conjunctiva and throat, and moderate enlargement of the cervical lymphnodes, but no strawberry tongue. The eruption disappears rapidly, and is followed by a very slight furfuraceous desquamation, lasting one or two weeks. There is little or no fever and constitutional disturbance. Full recovery without complications occurs rapidly. The contagious period appears to last two or three weeks.

This description is that of a disease with an efflorescence resembling that of scarlet fever, but in which the mildness or absence of other symptoms is suggestive of rubella. A very similar clinical picture is seen in certain mild cases of scarlet fever, occurring in certain epidemics, in which only the connection with other more typical cases proves them to be scarlet fever. Dukes, however, distinguishes his disease from scarlet fever on the ground that in the epidemics observed by him the clinical picture was frequently seen in children who had had scarlet fever, or in whom true scarlet fever occurred later. Furthermore, he found that all the cases ran a mild course without complications, and the incubation period appeared to be longer than in scarlet fever, namely, from nine to twenty-one days.

Filatow in 1886 had described the same clinical picture under the name of *rubeola scarlatinosa*, but he did not mean by this rubella with a scarlatiniform rash, but regarded it as a distinct disease. Many authorities have regarded the "fourth disease" as representing rubella with a scarlatiniform rash, and the long incubation period would well fit rubella. Dukes, however, was unwilling to admit the identity of the disease with rubella, on the ground that it frequently occurred in children who had had rubella.

Opinions differ as to the separate identity of Dukes' disease. The majority of authorities deny it, and regard the clinical picture as representing either a very mild abortive form of scarlet fever, or an atypical rubella with scarlatiniform rash. Others believe that Dukes' disease has a separate existence. In epidemics of rubella scarlatiniform rashes are not uncommon, but they usually involve only parts of the body, and a general scarlatiniform rash has hardly ever been described. In an epidemic in Philadelphia, described by Ostheimer, scarlatiniform rashes were seen, but were limited in extent. Also, the mildest scarlet fever cases usually show some features more characteristic of scarlet fever, than does the clinical picture described by Dukes. I have recently seen in the Infants' Hospital a case exactly fitting Dukes' description, but in which a recent exposure to scarlet fever could not be excluded. No further case occurred.

The question of whether Dukes' disease represents a separate

disease entity must be regarded as still open. It can only be solved either by the discovery of the causative organism, or by more extended epidemiological studies, or by hematological and serological research. For the safety of the community, cases presenting the clinical picture described by Dukes, should be treated as mild scarlet fever.

VARICELLA

(Chicken-pox)

Varicella is a contagious disease characterized by a vesicular exanthem, and mild constitutional disturbance.

ETIOLOGY. THE MICROÖRGANISM.—The cause of varicella, like that of most of the exanthemata, is as yet undiscovered. The virus does not appear to be contained in the vesicles, as, in contradistinction to variola, inoculation of children from the vesicles of varicella has not been followed by uniformly positive results.

TRANSMISSION.—Varicella is highly contagious. The contagium is usually air-borne, and the virus is extraordinarily light and easily carried in currents of air, so that it can cross a considerable air space. It is for this reason that the Germans call the disease “Windpocken,” and the French “petite vérole volante.” Transmission through the medium of healthy carriers or contaminated objects is rare, but has been known to occur.

The manner in which the virus leaves the patient, and the portal of entry are still unknown. It seems probable that it enters with the air in respiration.

The contagious period possibly begins shortly before the appearance of the exanthem. The infectivity is at its height at the beginning of the stage of efflorescence. By the time the vesicles appear, transmission to the other children in the family has already taken place. How long the contagious period lasts is unknown, but the infectivity appears to be slight at the time of the drying of the last vesicles. The longevity of the virus outside the human body appears to be short.

PREDISPOSITION.—The susceptibility to chicken-pox is very great. Usually when the infection enters a family for the first time, all the children are attacked. The disease confers a lasting immunity and second attacks are rare.

Varicella almost always occurs in childhood. The disease is very common up to the tenth year. Infants under three months are less often attacked than older children, but the disease can occur in the newborn. After the tenth year the number of cases becomes much less, and the disease is very rare in adults. The infrequency of chicken-pox in adults is, however, probably not due to a lessened

susceptibility, but to the fact that almost all persons acquire immunity through having the disease in childhood.

In general the disease is commoner in the colder months, probably because the schools are open and because housing conditions involve more intimate contact among children. The disease is prevalent at all times. Recognizable widespread epidemics are not seen.

INCUBATION.—The period of incubation in the majority of cases is fourteen days. It is almost never less than thirteen days, and may be as long as nineteen days.

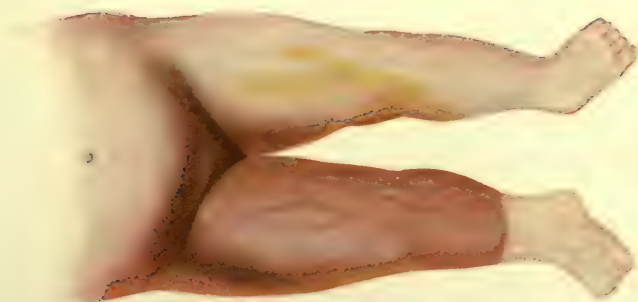
PATHOLOGICAL ANATOMY.—Deaths from varicella are so extremely rare that our knowledge of the pathology of the disease is necessarily limited. It is evident, however, that the efflorescence of vesicles, which represents the principal morbid lesion of the disease, is of a somewhat different type from that which occurs in variola. The vesicle is much nearer the surface than in the latter disease, being formed mostly by the upper layers of the epithelium. The vesicle itself is seldom multilocular, a condition which is frequently present in variola. The contents of the vesicles are usually a clear serum, the progression to a pustule being rare in comparison with the lesion of variola. The lesion so rarely involves the deeper layers of the skin, and the process is usually so very mild, that it is only in a few widely scattered lesions that sufficient destruction of the tissue takes place to produce a scar.

The lesions may appear on the mucous membranes as well as on the skin. At times the lesions assume a much more serious form and may become gangrenous. This occurs most often in poorly nourished, atrophic infants. In gangrenous varicella, the vesicles, instead of drying up in the ordinary way, become black and larger, so that a number of rounded, black crusts are scattered over the surface of the body. If a crust be removed, it is found to cover an ulcer more or less deep. Around it the skin is of a dusky red color. All the vesicles do not become gangrenous, so that we find crusts of the ordinary appearance mixing with the blackened crusts. The gangrenous process often penetrates deeply through the skin to the muscles. The lesions at times are so extensive as to form ulcers which may invade and destroy large areas of tissue.

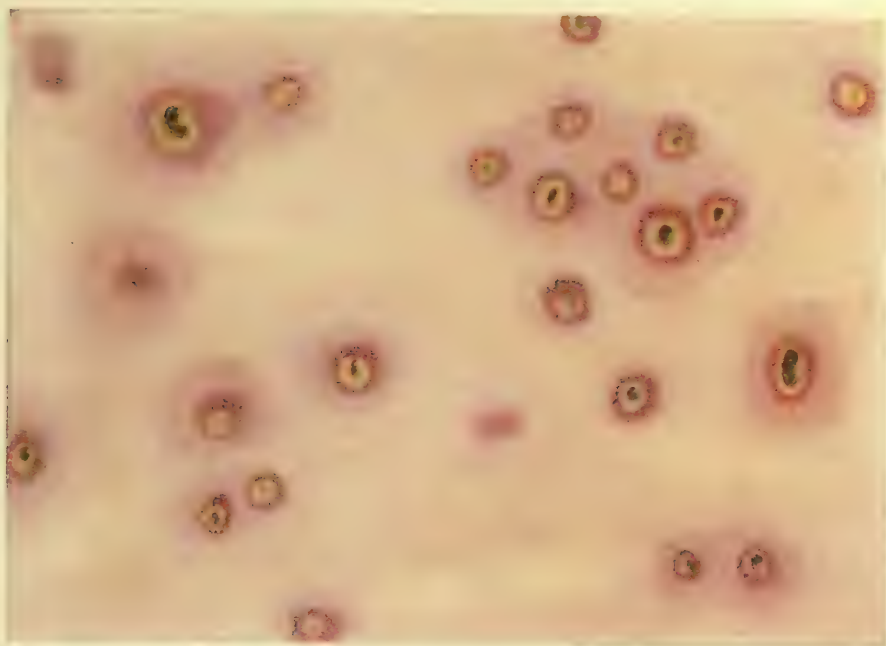
SYMPTOMS. PRODROMAL STAGE.—There are rarely any prodromata in varicella, beyond a slight malaise for a few hours. At times, however, especially in young infants, the onset of the disease may be severe; it may be characterized by vomiting, and, when the temperature is high, even by convulsions. In rare cases the prodromal stage is of considerable length and the prodromata resemble somewhat those of the other exanthemata.

EFFLORESCENCE.—The first symptom usually noted by the child's

PLATE XI.



Erysipelas.



Varicella.



Syphilis.

parents is the rash. This ordinarily appears first on the face and scalp, and soon appears on the body and extremities. It consists at first of small red spots about the size of the head of a pin. These rapidly increase in size, becoming papular, and about as large as a small pea. In the middle of a certain number of these papules appears a small vesicle, which quickly spreads, often covering the entire papule. The margin of some of the vesicles borders directly upon normal skin, while others do not involve the whole papule, and are surrounded by a reddened areola. The vesicles when fully developed are about the size of a small pea. Their contents are at

FIG 134



Varicella. Stage of efflorescence, third day

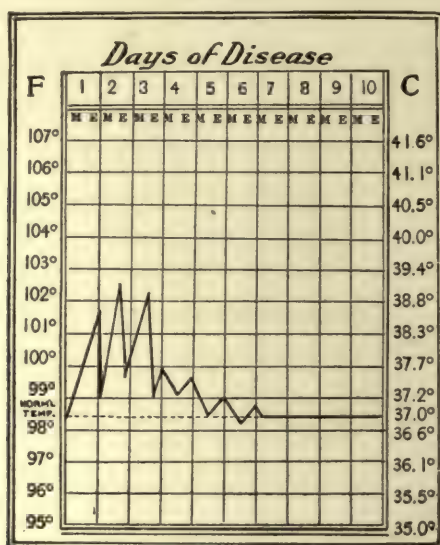
first clear, sometimes slightly cloudy, and later they become cloudier, but only occasionally become actually purulent. The vesicle is not umbilicated, and is unilocular. After one or two days it begins to dry up and flatten out, and in three to six days after its appearance it becomes a dry yellowish or brownish crust. These scales fall off at the end of the first or in the beginning of the second week, usually leaving no scar, unless the scab has been picked off prematurely by the patient.

It is characteristic of the disease that not all the lesions which appear go through all these stages. A certain number reach only the

macular or papular stage before fading, and never form the characteristic vesicles. Also new spots keep appearing for a number of days, or a week, many of which go through all the stages. Consequently at any time in the stage of efflorescence it is usually possible to see the lesions in all stages, macules, papules, vesicles, and crusts.

The number of lesions varies widely. Sometimes there are only a few, less than a dozen on the entire body, while at other times there are several hundred. On the face they can even become confluent. There is often a peculiar odor coming from the body, especially when the contents of the vesicles are very cloudy or purulent. During the crusting stage there is often itching, especially on the scalp, and the lesions may be infected by scratching, showing then more marked suppuration or the lesions of impetigo contagiosa.

CHART II



Varicella simplex

The eruption is frequently seen on the mucous membrane of the mouth and throat, involving most often the soft palate, but occasionally being seen on the tongue, pharynx and lining of the cheeks. The lesion on the mucous membrane is a rather large vesicle, but is rarely seen in this vesicular stage, as its covering becomes broken almost as soon as the vesicle is formed, and the usual appearance is that of a shallow greyish-yellow ulcer resembling the lesion of stomatitis herpetica.

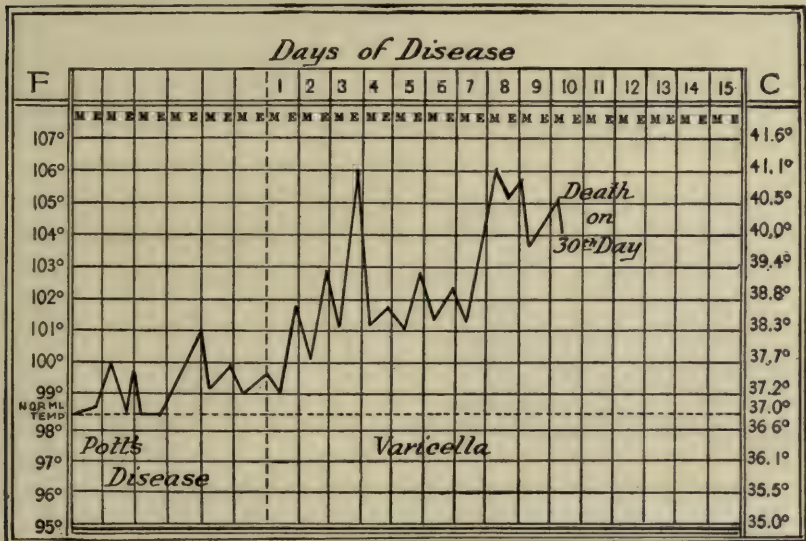
The eruption occasionally involves the nasal cavity, conjunctiva, and vulva. In the last situation itching is often severe, and scratching may cause troublesome secondary infection. In rare cases there

is involvement of the vocal cords, with hoarseness, croupy cough, and even symptoms of laryngeal stenosis.

OTHER SYMPTOMS.—The temperature in varicella is in most cases not high, and is very irregular. It usually rises when a crop of lesions of any considerable number develops, and falls again as they dry up. There is little or no constitutional disturbance in the majority of cases. There may be restlessness, disturbed sleep, and loss of appetite. In a few cases there is high fever, headache, and vomiting.

ATYPICAL FORMS.—In some very severe cases, the lesion may from the first be papular and hard like that of variola, the contents of the vesicles may become notably purulent, and they may be surrounded by a marked inflammatory areola. With such severe eruptions, the

CHART 12



Varicella gangrenosa

fever is higher, and the constitutional disturbance is much more severe. A markedly purulent eruption may leave scars. Over-clothing children tends to produce a more severe type of rash.

Occasionally single vesicles may reach an abnormally large size, resembling the lesion of pemphigus. The contents of the vesicles in rare cases is hemorrhagic. The vesicles are particularly apt to become pustules in poorly nourished infants, in subjects of eczema, and in the uncleanly.

A special type is sometimes seen, chiefly in ill-nourished children, which is called the gangrenous form of varicella. In these cases secondary infection of the vesicles causes large pustules, and the inflammatory process extends into the deeper layers of the skin and

subcutaneous tissue, and may even reach the muscles. The process causes gangrene of the skin. The lesions become covered with black crusts, which fall off, leaving deep, crater-like ulcers, often with a peculiar punched-out appearance. The process may lead to pyemia, metastatic suppuration, general sepsis, and death.

COURSE AND COMPLICATIONS.—The course of varicella is rapid. It is characterized by a sudden onset of mild constitutional symptoms, with the almost immediate appearance of the efflorescence. The efflorescence runs a rapid course, appearing quickly on different parts of the skin, and disappearing almost as quickly as it appears. The disease lasts about a week or ten days, and, as a rule, has no serious sequelae. It is rarely complicated by any other disease.

During the course of certain epidemics, however, it has been noticed that the *kidneys* are affected. This complication usually occurs after the efflorescence has almost disappeared, and in the second week from the time of the beginning of the attack. In these cases albuminuria is present, and in all probability is caused by some form of nephritis, although nothing definite is known about this class of cases.

DIAGNOSIS.—The diagnosis of varicella is not difficult if we bear in mind the characteristics of the diseases which it is most apt to simulate.

VARIOLA.—In differentiating it from variola we must consider the great difference in the rapidity of the development of the efflorescence in the two diseases. In variola it is essentially slow, in varicella it is characteristically quick. The papules of variola are hard to the touch, those of varicella are soft. The vesicle of variola, as a rule, is umbilicated and soon becomes a pustule; these characteristics are absent in varicella. The whole course of variola occupies a period of from two to three weeks; the course of varicella is much shorter, and is often limited to one week. Finally, the severe constitutional symptoms and the long prodromal stage in variola differ essentially from the lack of prodromata and the mild constitutional symptoms in varicella.

The following table gives the chief points of difference between varicella and variola:

TABLE 50

	VARICELLA	VARIOLA
Incubation.....	Two to three weeks.	One to two weeks.
Prodromata.....	None or slight.	Three to four days in length. Active. Severe.
Efflorescence.....	Rapidly becomes vesicular. Not umbilicated. Unilocular. Irregular. Lesions numerous. Universally distributed in successive crops. Vesicles differ	A slow progressive development from a macule to a papule, from a papule to an umbilicated vesicle, then to a pustule. Multilocular. Regular.

TABLE 50—*Continued*

	greatly in size. On pricking, collapses entirely.	Lesions not numerous. Defined in its localization. Lesions, as a rule, of uniform size. On pricking, collapses partially.
Desquamation.....	Slight crust formation.	Pronounced crust formation.
Duration.....	Short, one week to ten days.	Long, three to four weeks.
Type.....	Mild.	Severe.
Temperature.....	Irregular, not high.	Rises suddenly. Remains high until papules are developed, when it falls considerably. Rises again during the development of the pustules.

VACCINIA.—In vaccinia the slow progression of the lesions from papules to pustules, and the rather limited areas affected, serve to distinguish it from the successive crops of vesicles, with the rapid development and extensive distribution which are met with in varicella.

HERPES ZOSTER.—The differential diagnosis of varicella from herpes zoster is not difficult, if we consider that the vesicular efflorescence in herpes zoster follows the course of some set of nerves, while that of varicella is perfectly irregular and is in no way connected with the distribution of the nerves.

PROGNOSIS.—In the majority of cases, the prognosis of varicella is good. Severe cases are very rare. The only danger is in wretched atrophic children, in whom gangrenous varicella, and general sepsis sometimes develop.

PROPHYLAXIS.—When a case of varicella occurs in a family, it is well to isolate the patient. Although the disease is a mild one, there is always a possibility of a severe course, and I do not believe in ever intentionally allowing children to become exposed to a contagious disease. It is especially important to protect if possible young infants and sickly or poorly nourished children. In nine instances out of ten, however, isolation will be too late to prevent the spread of the disease to the other children. In children's hospitals, epidemics can only be prevented by closing the ward to new patients for three weeks after the last case.

TREATMENT.—The treatment of varicella is merely symptomatic. The child should stay in the house, and its room should be kept at an even temperature. The diet should be light. The child should be carefully watched to prevent it from scratching, as lesions deep enough to produce scars may often be obviated in this way. This treatment should be continued until all the constitutional symptoms have passed away and the efflorescence has disappeared. The skin should be kept clean. Itching may be relieved by sponging the skin with a solution of bicarbonate of soda, or a wash containing 1 per cent carbolic acid in lime water.

PROBLEMS AND RESEARCH. The only important problem in connection with varicella is that of the microorganism which causes the disease. The portals of entry and exit for the virus are also still in doubt. Some investigators have failed to produce any lesion in human beings by inoculation with the contents of the vesicle. Others have apparently obtained a local lesion. Kling has reported the attainment of a local lesion by inoculation which protected the children exposed from acquiring the disease, whereas 73 per cent of those exposed, but not inoculated, contracted chicken-pox.

VARIOLA

(Smallpox)

Smallpox is a specific infectious disease of unknown etiology. It is extremely contagious, and is characterized by a typical fever curve and a typical exanthem.

ETIOLOGY. THE MICROORGANISM.—The organism which causes smallpox has not been discovered. The most prevalent theory is that it belongs to the group of protozoa. It is known that the virus is contained in the vesicles, pustules and crusts which are formed upon the skin and mucous membranes. The virus is also present in any of the secretions and excretions which can become contaminated with the products of the exanthem or enanthem. There is evidence that the virus is sometimes contained in the blood.

The virus can pass through ordinary filters, but not through colloid filters. It is highly resistant to such injurious influences as light and drying, and is also resistant to disinfectants.

TRANSMISSION.—Both contaminated objects and droplet infection play a part in the transmission of smallpox. Not only can such objects as linen, clothing, and utensils which have been in contact with the patient, transmit the disease, but the contagium can also be carried on the skin, hair, or clothing of third persons who have been in contact with a patient. The contagium is also air-borne, dust and droplet infection playing a part, and there is evidence that the infection may be carried for a considerable distance through the air. It is possible that insects may help in the distribution of the virus.

PORTAL OF ENTRY.—The principal portal of entry is the mucous membrane of the respiratory tract, as the virus usually enters with the inspired air. The possibility of infection through the digestive tract cannot be excluded. When the contents of a smallpox lesion are inoculated into the skin, the resulting disease produced is never true smallpox, but consists in a local lesion, which was described by Brinckerhoff as a *variola inoculata*.

THE CONTAGIOUS PERIOD.—The disease is contagious at all stages, from the beginning of symptoms until after the completion of desquamation. The disease is most contagious during the stage of efflorescence.

PREDISPOSITION.—Mankind seems to be generally susceptible to smallpox. At all ages, however, some individuals appear to be insusceptible. The disease is commoner among children than among adults for the same reasons that explain the greater frequency of all contagious diseases in early life.

IMMUNITY.—One attack of smallpox confers an immunity which usually persists throughout life. There have, however, been rare recorded instances of second attacks. The immunity conferred by variola inoculata or vaccinia, is not so persistent.

PATHOLOGICAL ANATOMY.—The pathological conditions found in variola are chiefly those of the skin and the mucous membranes. The lesion begins as a round, somewhat raised macule, which develops into a hard papule, and later a small vesicle arises on its summit. This vesicle enlarges very rapidly and changes to a tensely filled pustule with a central depression. The size of this pustule corresponds to that of the original macule. Microscopically the macule consists of a circumscribed spot of hyperemia in the capillary layer of the skin. The papule is formed by a sharply defined necrobiotic degeneration of the under layers of the rete mucosum, by which process the nuclei of the epithelial cells are destroyed. By the transudation of fluid into these areas the cells are pushed apart and the epithelial layer is filled up as a whole, covering the area affected, and forming a vesicle, the inner part of which is composed of a mesh-work filled with lymph. In the vicinity of the necrobiotic focus, an inflammation is set up, causing an increased growth of the cells of the rete which surround the cells of the focus on all sides. The developed pustule extends through the whole thickness of the cutis to the subcutaneous tissue. A net-work inside the pustule, which is most tense in the central part, connects the roof and the floor of the pustule, and, in conjunction with the above-mentioned growth of the cells of the rete around the focus, causes the central depression. If the vesicle is pricked, only a part of the lymph flows out of the mesh-work within. The lymph contains some white and red blood-corpuscles, streptococci and staphylococci, fibrin-floculi, and molecular granules. The contents of the pustule are purulent, and those of the hemorrhagic variety contain blood. Clumps of bacteria with corresponding localized degeneration and its associated changes are found in the neighborhood of the pustules, also in the parenchyma of the internal organs and lymph-glands, as well as in the skin. These secondary infections are largely responsible for the

stage of pustules and for the toxic symptoms. The severe hemorrhagic and malignant forms are probably dependent more upon the activity of the secondary streptococcus and staphylococcus infections than upon the primary infecting agent. When the lesion of variola has reached its height, the central depression in the pustule disappears, because the increased tension in the contents tears away the meshwork. The vesiculation begins in the upper central part and spreads downward towards the periphery. The pustule then collapses and changes to a crust, which after a certain number of days falls off, leaving a more or less deep scar covered with young epithelium. If the suppuration extends into the deeper layer, scarring invariably results; it does not necessarily follow if the suppuration is confined to the upper layer. A distinct difference in the anatomy of a pustule of variola vera and one of varioloid does not exist.

On the mucous membrane of the mouth, nose, conjunctivae, bronchi, esophagus, rectum, sometimes of the vagina, and also on the tonsils and the tongue, the same pustular efflorescence may be found, and is either superficial or extends more deeply. At times also a pseudo-membrane is found on the ulcers.

In the intestines, swelling of Peyer's follicles is not uncommon. In the larynx, the efflorescence may be associated with a fibrin exudate, and sometimes with edema sufficient to cause death. Occasionally the inflammation extends deeper and involves the cartilages. In the trachea and bronchi there may be ulcerative erosions, but the characteristic lesions seen on the skin do not occur. There are no special lesions of the lungs, but congestion or broncho-pneumonia is very common.

Conjunctivitis, keratitis, and inflammation of other parts of the eye may occur in the course of the disease or afterwards.

Acute otitis media, with or without suppuration, is of common occurrence.

The pathological changes in the other organs consist of enlargement of the spleen and fatty degeneration of the liver, kidneys, and heart. Metastatic processes in the various organs and in the joints sometimes occur. In the hemorrhagic form, hemorrhages in the various cavities, in the different organs, and, according to Golgi, in the medullary cavities of the bones, may occur, also on the serous and mucous surfaces and in the muscles. The blood shows an active leukocytosis during the pustulous stage.

INCUBATION.—The incubation of the disease varies from twelve to fourteen days, the latter being the most frequent period.

SYMPTOMS.—According as the symptoms of variola are mild or severe, the disease has been divided into a number of forms, designated as follows: (1) *Discrete*, (2) *confluent*, (3) *hemorrhagic*, and

(4) *modified*. In all these forms the initial fever, convulsions, and general symptoms may be severe, and do not necessarily indicate which type of the disease is about to follow.

The mildest and most typical form of the disease is that which is called *discrete*.

PRODROMATA.—In this form, the invasion, although sometimes less severe than in the confluent and hemorrhagic forms, is in infants and young children almost always of a grave type. In infancy and early childhood the disease commonly begins with convulsions. There may be vomiting, great restlessness, rapid pulse, high temperature, and in a number of cases the children quickly succumb to the disease from the virulence of the toxemia. If they survive this early stage of the disease they usually present the same sequence of symptoms as in cases occurring in later life, but may eventually die from the exhaustion which often rises from a prolonged suppurative fever. In the prodromal stage the pulse is much accelerated and the temperature may be as high as 104°, 105°, or 106° F. In this stage we at times, especially among children, meet with an evanescent erythematous efflorescence. It has a peculiar distribution and generally a limited extent, usually affecting the lower abdominal areas, the inner surface of the thighs, the sides of the thorax, and the axillae; sometimes, however, it involves the whole surface. This efflorescence is distinct from the typical lesions of variola which occur later.

EFFLORESCENCE.—On the third or fourth day of the prodromal symptoms an efflorescence appears on the skin, and at this time the frequency of the pulse lessens, the temperature usually falls considerably, and the more severe symptoms improve, so that the patient appears much more comfortable. The efflorescence is at first represented by small red macules or papules, which, as a rule first appear on the forehead, or on the face and mucous membranes, and later on the trunk and limbs. The papules are rather scattered in their distribution, and have the feeling of shot under the skin. The macules when present soon become papules. On the third day by means of a good light a small vesicle can be seen at the apex of the papule, and by the fifth or sixth day the vesicular stage is well established and the vesicle becomes distinctly umbilicated. This appearance on careful examination can also be seen in the lesions of the mucous membranes. At about the eighth day the vesicles become pustules, the tops soon flatten, and the umbilication disappears, leaving an areola of injection and the intervening skin in a swollen condition.

TEMPERATURE.—The temperature at this time rises, from the supuration which is taking place in the pustules. This rise of tem-

perature is called the secondary fever, or fever of suppuration. The temperature remains high for from twenty-four to forty-eight hours, and then gradually falls until by the twelfth or thirteenth day it usually becomes normal. The contents of the pustules dry up, and crusts are formed. On the palms and soles small hard disks form, which may of themselves fall off in infants, but in children as old as ten years would remain for a long time unless removed with the point of a knife.

BLOOD.—On examining the blood in cases of variola, Arnheim found the hemoglobin diminished at the beginning of the disease. After the formation of pustules and during their exsiccation, he found an increase of the hemoglobin with diminution of the erythrocytes. When complicating suppuration occurred, both the erythrocytes and the hemoglobin remained for a long time abnormally diminished.

Pick, in forty-two cases found no leukocytosis except in the stage of suppuration or in some complication like pneumonia. This was the case even when the temperature was high, the disease severe, and the termination fatal.

DESQUAMATION.—By the fourteenth or fifteenth day the stage of desquamation is established. In some cases extensive scars are left on the skin where the crusts have fallen off. This is more apt to occur in severe cases.

CONFLUENT FORM.—In contradistinction to the mild or discrete form of variola is the more severe form, called *confluent*, on account of the tendency of the lesions to coalesce. In the confluent form of variola the efflorescence usually appears at the same time as in the discrete form. At about the fourth day the lesions become confluent, the skin becomes reddened and swollen, and the face may be much distorted by the severity of the eruption. In this form the initial temperature does not fall to the same degree as it does in the discrete form, and diarrhea is likely to occur, particularly in children. The pharynx and larynx are especially apt to be involved, and the cervical lymphnodes to be enlarged. The crusts adhere longer in the stage of desquamation than they do in the same stage of the discrete form.

HEMORRHAGIC FORM.—The third or *hemorrhagic* is the most virulent form of variola, and may occur in children as it does in adults, although not so frequently in the former as in the latter. Its symptoms in children are so severe that in almost every case it very quickly proves fatal. It is characterized by punctiform hemorrhages in the skin, appearing from the first to the fourth day of the prodromal stage, ecchymoses in the conjunctivae, and hemorrhages from the mucous membranes. According to Osler, hematuria is the most common form of hemorrhage, hematemesis the next.

MODIFIED FORM.—The fourth or modified form of variola occurs when the disease attacks individuals who have been successfully vaccinated. This form is called *varioid*, but would be better termed *modified smallpox*. Modified smallpox is usually much milder in its symptoms than any of the other forms of variola, although the initial fever may be as high as in a severe case. The lesions are fewer in number, the temperature becomes normal sooner, and the child seems comfortable in a shorter period of time, since there is usually no secondary fever from suppuration. The nearer the attack comes to the time when the child was vaccinated, the less severe will be the symptoms.

In any of these forms of variola the prodromal symptoms may be of a very severe nervous type, and this is especially characteristic of the disease as it occurs in children. For this reason variola may simulate other diseases in its prodromal stage, and may often cause death before the efflorescence has appeared. This is especially the case with the prodromal symptoms of the hemorrhagic form.

COMPLICATIONS.—The most common complications of variola are those of the larynx and the lungs. When the larynx is affected, edema of the glottis may suddenly arise and death take place from suffocation. When a lesion of the lung develops, it is usually in the form of a bronchopneumonia.

In the throat, the presence of the efflorescence occasions great irritation, and the accompanying secretions cause nausea and at times dyspnea, with a cough which in weak children is very exhausting.

When acute inflammation of the middle ear has taken place, the pain during the formation of the pus is very intense, but it subsides as soon as the sac bursts or is incised. This complication, therefore, requires early and careful treatment.

Although albumin is very frequently present in the course of the disease, nephritis is rare.

DIAGNOSIS.—There is no other acute infection accompanied by an efflorescence on the skin which in a typical case would be likely to be mistaken for variola. The severe constitutional symptoms, the slowly developing and rather scattered macules and papules, with the shotty feeling of the latter, the umbilicated vesicles gradually becoming pustules, the extensive crust formation, and the initial and suppurative fevers all render the diagnosis in most cases quite plain.

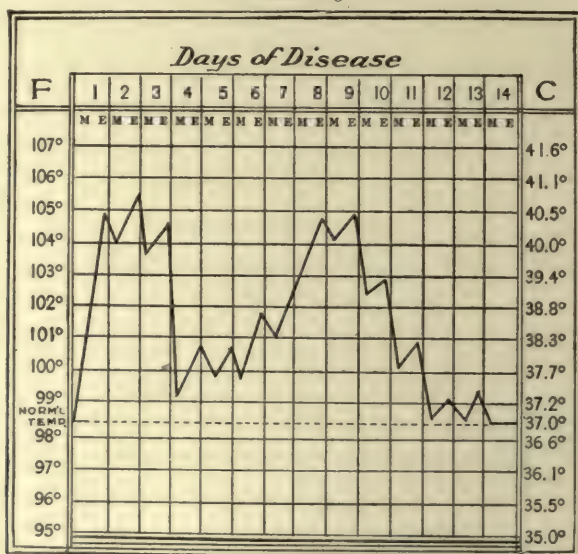
Extreme cases of varicella have been mistaken for variola. The differential diagnosis between the two diseases is given in the table under varicella.

Variola differs materially in its prodromal symptoms from measles, in which the pronounced catarrhal symptoms of the nose and eyes

make the differentiation comparatively easy. Although the prodromal symptoms of scarlet fever and of variola, such as the convulsions and vomiting, are often of equal severity and somewhat similar, yet the pronounced symptoms connected with the throat in scarlet fever, and the appearance of an erythematous efflorescence, instead of the scattered papules of variola, serve to differentiate clearly the two diseases. We must, however, be careful not to mistake the evanescent efflorescence which occurs in the prodromal stage of variola for the erythema of scarlet fever. The distinction can usually be made by remembering that the efflorescence in variola has the peculiar distribution described under prodromata, while the typical location of the efflorescence of scarlet fever is first on the neck and chest.

The following chart represents the usual temperature curve:

CHART 13



Fever of invasion. Fever of suppuration. Variola

In making the diagnosis of variola we must bear in mind the efflorescence which appears on the skin in the course of a general *vaccinia*. In vaccination the single lesion and the absence of severe constitutional symptoms make it hardly necessary to do more than refer to it in this connection. The differential diagnosis from general vaccinia is not difficult, and yet general vaccinia is so rarely met with that when it appears it almost always creates a suspicion that we may be dealing with variola. As a rule, in vaccinia the general symptoms are not severe, the disease being represented almost entirely by a slight malaise and loss of appetite, in conjunction with

the appearance on the third or fourth day of an efflorescence on the skin, represented by papules, vesicles and pustules, few in number and irregularly distributed, some on the face and nose, and a few on the body and extremities. As these manifestations almost invariably appear after vaccination, this fact is of great aid in the differential diagnosis from variola. The subsequent course of a case of vaccinia is so much milder and shorter than that of variola that in a few days the differential diagnosis can easily be made.

PROGNOSIS.—The prognosis of variola depends upon whether the child has been vaccinated, and also upon whether children who have been vaccinated when infants have been revaccinated. In the unvaccinated the prognosis is always bad, and is proportionately grave the younger the child. In the vaccinated the prognosis is good, and is favorable proportionately to the shortness of the interval between the invasion of the variola and the time of the previous vaccination.

TREATMENT.—There is no specific treatment for variola, but it is of the utmost importance that the best hygienic care should be employed. The air of the room should be perfectly fresh. The crusts should be kept softened with a mixture of glycerin, oil, and carbolic acid, and the odor arising from them should be modified by the application of a dilute solution of carbolic acid. The general principles of treatment are the same as in any severe acute infection.

In the initial stage of the disease, stimulants should be given freely if the symptoms are severe, and the high temperature should be controlled by sponging with water at a temperature corresponding to the power of the child's reaction.

The greatest care should be taken during the stage of convalescence, and when the child is considered well the most rigid measures for preventing the spread of the contagion should be enforced. The clothing and everything connected with the child and its attendants, and the room in which they have been kept during the sickness of the child, should be thoroughly disinfected, the same precautions being taken to prevent the spread of variola as in scarlet fever. The immediate transfer of a patient from its room to a smallpox hospital is in most communities considered the wisest method of dealing with the disease, and is usually enforced by law.

VACCINIA AND VACCINATION

(Cowpox)

Vaccinia is a specific eruptive disease occurring in cattle, especially in cows. It is a question whether cowpox represents a separate disease, or is smallpox modified by animal passage. Authorities differ

on this point, but the weight of modern opinion inclines to the view that vaccinia is modified smallpox. The disease in human beings may be either a local affection spreading from a point of inoculation, such as from vaccination, or may rarely be a general manifestation. It is the latter condition which is usually meant by the term vaccinia as applied to human beings. It has been supposed that vaccinia may occur by the introduction of the vaccine lymph into the blood, but it is now believed that the generalized eruption is caused by auto-inoculation. The disease is characterized by the appearance of papules, vesicles and pustules of different sizes in different parts of the body and limbs, as well as on the face, and running a definite course. It may be said to be a rather rare disease. When its lesions follow vaccination, they appear at about the fifth day after the inoculation. At the end of four days, however, minute vesicles can be seen with the magnifying glass.

VACCINATION.—By vaccination is commonly meant artificial inoculation with the virus of vaccinia as a preventive against variola. During a period of fifteen years no death occurred from variola in Boston of a child who had been vaccinated before it was five years old. During the same period the percentage of deaths among the unvaccinated at the Boston Smallpox Hospital was 75 per cent, while that of the vaccinated was 3 per cent. For the past seventeen years no person who has been successfully vaccinated within five years has died of variola, and those who have been attacked by variola have had the disease in a very mild form. In order to show the relative frequency of deaths occurring in the vaccinated and in the unvaccinated, I have arranged the following table, based on a report by Dr. Barry of an epidemic of variola at Sheffield, England, during 1887 and 1888. The table shows the percentage of those who, living in houses invaded by variola, were attacked by the disease, and also how many of these died. It also gives the percentages for all ages, and for those under ten years and over ten years.

TABLE 51

Individuals Living in Houses Invaded by Variola.

	1	2	3
	ALL AGES	OVER TEN YEARS,	UNDER TEN YEARS,
	PER CENT	PER CENT	PER CENT
Vaccinated.....	{ Attacked..... 23.0	28.1	7.8
	{ Died..... 1.1	1.4	0.1
Unvaccinated.....	{ Attacked..... 75.0	68.0	89.9
	{ Died..... 37.2	37.1	38.1

The low percentage of children as shown in column 3 is very striking in comparison with column 2, which represents older individuals,

and emphasizes the importance of revaccination. It also impresses upon us the significance of the difference in the number of deaths between the vaccinated and the unvaccinated. When large numbers of cases of variola have been reported, figures show that among the vaccinated nineteen out of twenty recover, while of the unvaccinated fifty individuals out of one hundred die. It is therefore evident that vaccination is highly protective against variola, and physicians should insist on the vaccination of every individual in the community. One vaccination, however, does not protect for a lifetime. On the contrary, revaccination is just as important as the primary operation.

Revaccination should be performed at intervals of eight or ten years, *and in a shorter time when cases of variola appear in the community*. The danger of serious results arising from vaccination is extremely small.

The time at which vaccination should be done is of considerable importance. The infant should be vaccinated early, before it begins to be exposed to the danger of contagion from sources outside of its home. We must, however, remember how low is its vitality at birth, and how readily this vitality is affected by what would be considered trifling conditions in the older child or in the adult. A time should be chosen when the infant is not subject to the other disturbing conditions which naturally arise in the first two years of life, such as weaning and the irritation of the dental periods. If it is found necessary to vaccinate the infant after the sixth or seventh month, or before the twentieth, it should be done in an interdental rather than in a dental period, and not at the time when its food is being changed, or when it is suffering from either slight catarrhal conditions or some definite disease. I prefer to vaccinate the infant when it is four or five months old, that is, just before the period when the first tooth appears. At this age it has usually become accustomed to its food, its digestion is in equilibrium, and its vitality is much above what it was in the early weeks of its life. By the fifth month also, it will usually have developed the outward symptoms of syphilis if it has inherited that disease from its parents.

The vaccine virus can be introduced into any part of the body through the skin according to the fancy of the physician or parents. Girl infants can be vaccinated just below the knee on the outer side of the leg, so as to avoid having on the arm a scar to which women usually object. We are accustomed to vaccinate boys on the outer side of the upper arm. Whether the vaccination is performed upon the leg or the arm, we should first inquire if the person who is to take care of the infant is right-handed or left-handed. If the nurse, for instance, is right-handed, she will naturally hold the infant on her left arm. and in this case, the infant's right arm being towards the nurse, it is better for the vaccination

to be on the left arm. The process should be reversed when the nurse is left-handed, and in this case, for the same reason, it is better to vaccinate on the right arm or leg. The form of virus which I have been accustomed to use is lymph obtained from cows, put up by the State Board of Health. It is essential to use vaccine known to be good, and put up under the best conditions. It should be very carefully prepared by those who have made a scientific study of the subject, and, if possible, on farms which are under state supervision. A very small surface is amply sufficient for the proper introduction of the virus. A pointed ivory quill charged with glycerinated lymph (such as is shown in the plate), was formerly used for removing the epithelium, for exposing the smaller blood-vessels, and for introducing the virus. The vaccine is now, however, generally put up in sterilized glass capillary tubes. An ordinary glover's needle is preferable to the quill for removing the epithelium. It can be sterilized by being held for a moment in the flame of a match or candle, and then wiped on sterile gauze.

The utmost precaution should be taken to insure against infection from other microorganisms. The part of the skin chosen for the vaccination should be thoroughly washed with soap and water and with alcohol. The hands of the operator should be clean and aseptic. A series of short scratches should be made about one-half centimeter (about one-fourth inch) long, until the epithelium is sufficiently removed to show that the blood vessels are exposed, but not to a degree sufficient to cause bleeding, for in the latter case the virus may be prevented from gaining an introduction to the tissue. The capillary tube is then broken, and the lymph allowed to run on the abrasion, and rubbed in with the side of the needle. The skin should be protected for four or five minutes from contact with anything and then covered with a sterile gauze pad held in place by adhesive plaster. The plate shows the different stages of a vaccination as they occurred in one case carefully observed by the artist every day.

Every case of vaccination does not present exactly the same appearances. The lesions may differ in shape and size, and one individual may be affected more intensely by the virus than another; one may have accompanying severe constitutional symptoms and another may have none. The chain of lymphatics may be affected as far as the axilla or the groin.

The following description represents pretty well the usual course of the disease. After the vaccination, the skin shows nothing new until the third, fourth, or even the fifth day, when a red point appears. This soon becomes a papule; by the next day a vesicle has developed; about the sixth day this vesicle usually becomes umbilicated, and is surrounded by a faint red zone. By the eighth

PLATE X.



Capillary Glass Tube.



Vaccination Scratch.



At 5th Day.



At 8th Day.



At 10th Day.



At 12th Day.



At 16th Day.



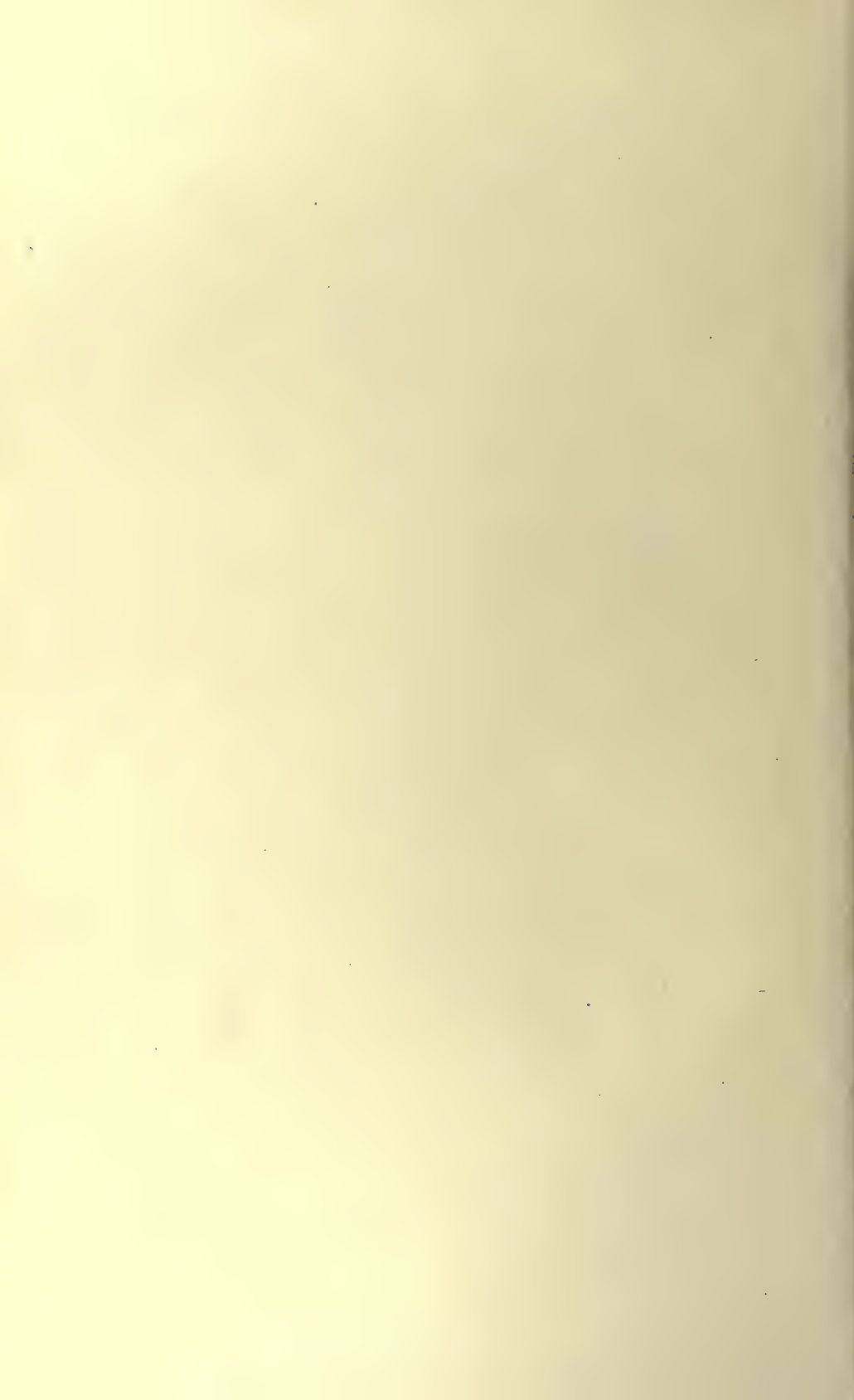
At 19th Day.



Scar at 1 Year.



Scar at 21 Years.



day the vesicle is fully developed, and by the ninth day the red zone increases rapidly and the vesicle soon becomes a pustule. By the eleventh or twelfth day a crust is formed, and this crust falls off from about the fourteenth to the twenty-first day. In some cases an ulcer is left which heals by the formation of another crust, in others the skin remains intact. From the eighth to the twelfth day there may be a slight amount of fever and a coated tongue, with some loss of appetite, and the glands of the axilla or groin may become enlarged and tender. The scar, although perhaps not typical, can usually be recognized by its small depressions (pits) and its location.

In some cases, instead of the healing of the scratch in a few days, or the formation of the vesicle of a successful vaccination, irregular excrescences of a fungus-like character may appear. These in all probability have no connection with the vaccine virus, and are not protective. In addition to the rather rare cases of vaccinia, various efflorescences at times appear on the skin, not only in the neighborhood of the vaccination lesion, but also in other parts of the body. They may be present on the fourth or fifth day, or even later, in the second week, and are probably caused by some toxic substance connected with the vaccination lesion. They vary considerably in form, but are usually represented by a multiple or papular erythema or an urticaria.

II. HIGHLY CONTAGIOUS DISEASES WITHOUT EXANTHEM

This group includes infections which resemble the exanthemata in that they are transmitted very easily from one individual to another by contact, but do not show a characteristic cutaneous efflorescence. The diseases of this character are diphtheria, pertussis, mumps and influenza.

DIPHTHERIA

Diphtheria is a contagious specific infection, caused by a known microorganism, and characterized by a membranous inflammation of the mucous membranes, particularly of the throat and upper air-passages, and by certain more remote effects of the action of a soluble toxin produced by the organism.

ETIOLOGY. THE MICROORGANISM.—Diphtheria is caused by a bacillus, which was first described by Klebs in 1883, and was found to be the specific cause of diphtheria by Löffler in 1884. It is usually called the Klebs-Löffler bacillus. It has been isolated in pure culture, inoculations with which reproduced the essential lesions of the disease in animals. The bacillus secretes a soluble toxin, which has been isolated from cultures, and with which the general toxic lesions of diphtheria have been reproduced in animals.

The Klebs-Löffler bacillus shows great variations in morphology, growth, and virulence. The typical bacillus is a straight rod about the length of the tubercle bacillus, but decidedly thicker. It is easily stained by the aniline dyes, particularly by methylene blue. It is apt to stain irregularly, presenting an appearance suggesting spores. The stain may also give it a bipolar appearance. Long involution forms are frequently seen.

The organism grows rapidly on Löffler's blood serum, moist grey colonies appearing in sixteen to twenty-four hours. It resists cold, but dies when heated at a temperature over 56° C. It may remain alive outside the body for a considerable time when conditions are favorable, namely, moisture and darkness. It dies in sunlight.

The organism is found chiefly in the necrotic or inflamed tissue of the membranous lesion. In certain cases it has been found in the cervical lymphnodes, lungs, cerebrospinal fluid, blood and urine.

The organism remains upon the mucous membrane after the disappearance of the local lesion for a varying time which may reach many weeks. During this time it may retain its virulence. The organism may reach the mucous membrane without producing a

lesion or clinical diphtheria, but nevertheless retaining its virulence. Many healthy persons, especially those who have been in contact with a case of diphtheria, have virulent Klebs-Löffler bacilli in their noses or throats. Such persons are called "*diphtheria carriers*"

There is also frequently found in the noses and throats of healthy persons a bacillus which morphologically bears a close resemblance to the Klebs-Löffler bacillus, and which is called the *pseudo diphtheria bacillus*. This form is distinguished with certainty from the true organism only by the effect of animal inoculation. It does not produce diphtheria, and represents an avirulent type of the Klebs-Löffler bacillus.

TRANSMISSION.—Diphtheria is transmitted from a patient having the disease to a healthy person. The connection is not always close, however, owing to the fact that both convalescent and healthy persons may be diphtheria carriers. A healthy carrier may receive the organism from a diphtheria patient, may carry it indefinitely, and then may transmit it to a third person in whom it produces the disease. Diphtheria is, however, most commonly transmitted directly without the intervention of a healthy carrier.

Diphtheria is a contact infection. The individual who contracts the disease must in the majority of cases come into actual contact with the diphtheria patient or carrier, or with an object contaminated by the secretions of the patient. The contagium is not usually airborne, as the big, heavy diphtheria bacillus is not very volatile. Only when the patient coughs or sneezes directly in the face of the susceptible individual is the contagium carried through the air on the moist drops expelled from the patient. Usually close contact is required. As the bacilli live in the mouth, and come in and go out through the mouth, kissing is a common form of contact by which the disease is transmitted. The hands, bed and clothing of the patient are easily contaminated by secretions, and from these the hands of the second individual may be contaminated by contact, and then convey the contagium to the mouth. The bacilli are also frequently carried over by contaminated objects such as handkerchiefs, playthings, articles of food and the like.

The mode of transmission of diphtheria does not resemble that of measles, rubella and varicella, but is in every way similar to that of scarlet fever. Crowded conditions of life and uncleanness favor the spread of the disease, which is easier among the children of the proletariat than of the well-to-do.

The diphtheria bacilli, after transmission as described, usually enter the mouth with the fingers or food, and are most apt to develop upon the tonsils or soft palate.

TOXIN FORMATION AND IMMUNITY.—The lesions of diphtheria, both

local and general, are due to the action of a soluble toxin secreted by the bacilli. Whether or not all the lesions are produced by a single toxic substance, or by more than one, is an open question. There is evidence in favor of the theory of Ehrlich, that the local lesion and general poisoning are produced by the toxin, while diphtheritic paralysis is produced by the toxone. Recovery takes place through the formation by the cells of the body of a substance which neutralizes the toxin.

This immune body is consequently an *antitoxin*. Infection with diphtheria does not produce a permanent immunity. The immune body appears to become used up in some way, as second or even third attacks of diphtheria are not at all uncommon. The immunity produced by serum treatment is neither permanent nor long lasting.

There is a *natural immunity* to diphtheria, which lasts longer than the immunity produced in a patient who undergoes the infection. It has long been known that a certain proportion of children are immune to diphtheria, and the majority of very young infants are known to be immune. This immunity has been found to be due to the presence in the blood of a supply of diphtheria antitoxin. Whether or not this antitoxin has resulted from active immunity in the ancestors is not known. The amount of natural antitoxin in the blood may be estimated by an animal test (Römer's intracutaneous method on guinea-pigs), but this method cannot detect less than 1.16 units of antitoxin in 1 c.c. of serum, and less than this amount has been proven sufficient to produce immunity. Schick has described a method of determining natural immunity for routine use.

The Schick test for susceptibility to diphtheria consists in injecting into (not under) the skin a very small amount of diphtheria toxin, the quantity used being one-fiftieth of the minimum lethal dose for a guinea-pig weighing 300 grams. The toxin is so diluted that this dose is contained in 0.1 c.c. of fluid. This is injected into the skin of the forearm with a small needle. If properly made the injection should produce a small, raised, white spot. Within twenty-four hours, if the reaction is positive, the area becomes reddened, slightly edematous, and slightly cyanotic. This passes off in forty-eight hours, leaving a brownish pigmentation. The reaction is positive only in individuals without antitoxin in their blood, and means that they are susceptible to diphtheria. A negative reaction indicates that the individual has one-thirtieth of a unit or more of antitoxin in 1 c.c. of blood, and is immune. Children sick with diphtheria give a positive reaction before antitoxin is given.

The Schick test is of great value in determining whether children who have been exposed to diphtheria, or who are admitted to the open wards of a hospital, require an immunizing dose of antitoxin.

Only those with positive reactions need be immunized. It has been determined that the artificial immunity produced by antitoxin, and by the disease itself, is very varying in length, but does not usually last more than three weeks. The value of the Schick test has been confirmed by Park and his associates, and by other observers.

PREDISPOSITION.—The general susceptibility to diphtheria is much less than toward measles, chicken-pox and whooping-cough, and probably less than toward scarlet fever. The Schick test has confirmed the clinical observation that a certain proportion of children are immune. According to Schick's observation 93 per cent of the newborn are protected by natural antitoxin, 57 per cent of children in the first year, 37 per cent of children between two and five years, and 20 per cent between five and fifteen. In two years at the Infants' Hospital in Boston, where the Schick test is performed as a routine on admission, about 60 per cent of children under two years were found immune, the majority being in the first year.

Adults show a much smaller proportion having natural immunity than children, but yet diphtheria is much commoner in childhood. The frequency of the disease in children is not due to greater susceptibility, but to the same reason which causes all of the contagious diseases to attack children more than adults, namely, that the conditions of life in childhood favor the spread of all diseases acquired by close contact.

Diphtheria is most common between the ages of two and five years. It is infrequent after ten years. Among individual predisposing causes are adenoids, enlarged tonsils, and a tendency to catarrhal affections of the mucous membranes. For this reason the disease is seen more often in autumn, winter and spring than in summer. There are other factors. Certain children seem to have an individual constitutional predisposition. The chances of infection and the severity of the case depend not only on the constitutional predisposition, but upon the virulence of the particular diphtheria bacilli causing the disease.

EPIDEMIOLOGY.—Sporadic cases of diphtheria are seen at all times. The frequency of the disease varies from year to year. At times the prevalence of the disease is such that it amounts to a more or less widespread epidemic. The contagiousness and severity of the disease tend to increase with the frequency of cases, and are greatest in epidemics.

INCUBATION.—Diphtheria, unlike the exanthemata, has no definite period of incubation. The disease may appear within twenty-four hours of exposure, or may not appear for two or three days.

PATHOLOGICAL ANATOMY.—The lesions of diphtheria are due to the local action of the Klebs-Löffler bacillus and associated

bacteria, and to the absorption of toxins produced by the bacteria. The most constant lesion is a pseudo-membrane, produced by the local action of the bacilli in the upper air-passages, and due to exudation and coagulation necrosis. The exudation coming from the vessels of the tissue beneath the membrane meets the necrotic tissue containing a fibrin ferment, and coagulation takes place, the fibrin of the coagulum being intimately associated with the necrotic epithelium. The bacilli can also produce other lesions, such as simple inflammation, necrosis without membrane formation, and even abscess. There is no pathological condition directly characteristic of the action of the Klebs-Löffler bacillus, and the same anatomical conditions may be caused by other bacteria, and even by irritants. The process may rarely be simply a catarrhal inflammation, which does not go on to the formation of a pseudo-membrane.

The primary infection in diphtheria is most commonly in the throat, from which the bacilli may extend to the adjacent mucous surfaces, producing in most cases, membrane formation, in some only catarrhal or purulent inflammation. They may also extend into the nose, producing nasal diphtheria, or along the Eustachian tubes into the middle ear, or from the nose into the accessory sinuses, downward into the trachea and air-passages, or into the esophagus and stomach. There are certain differences in the membrane formation due to the anatomical character of the tissue. Thus the membrane in the pharynx clings tightly to the surface, while in the trachea and lower passages it is easily removed.

The extension of the bacilli into the lungs may produce a membrane formation in the smaller bronchi, areas of bronchopneumonia or even abscesses. The pathological process may be further modified by the association with the Klebs-Löffler bacillus of the common pyogenic cocci, and it is difficult to determine exactly the part which these various organisms play in the production of the local lesions. It is certain, however, that the lung lesions which are ordinarily attributed to these associated organisms may be produced by the Klebs-Löffler bacillus alone.

The membrane in diphtheria is usually of a peculiar greyish-white color and, as a rule, cannot be easily detached; in some cases, on the contrary, it may be white and easily separated. It sometimes assumes, early in the disease, a gangrenous appearance, which shows that the case is serious. Nasal diphtheria is characterized by a profuse nasal discharge, and often by a membrane. Transmission of the germ of the disease from the nose to the eye is infrequent, and does not always result in the formation of a false membrane. Frequently the pharyngeal inflammation extends through the Eustachian tube, causing inflammation of the middle ear, and in these cases a membrane may be formed. The membrane may extend downward

to the larynx, causing marked dyspnea. Below the vocal cords the membrane is not very firmly attached, and is frequently coughed up. If death occurs late in the disease or in apparent convalescence no macroscopic lesions, as a rule, are found. Microscopic examination of the nerves, however, often shows marked degeneration of the nerve tissue.

The internal lesions of the disease are not due to the presence of the bacilli but to the action of the toxic substances which are absorbed from the places where the bacilli are growing. These lesions consist chiefly in diffuse degenerative changes, and in intense local processes, also of a degenerative character. The organs most commonly affected by these lesions are the kidneys and the lymphnodes. The adjacent lymphnodes are apt to be swollen, and on microscopical examination they often show small foci of cell-necrosis; similar smaller necrotic foci may be found in other parts of the body, as in the liver, and are due to absorption of toxins. There is also a general lymphatic hyperplasia, which is relatively greatest in the abdomen. The kidneys ordinarily show only parenchymatous degeneration, but in a few cases of recurrent infection they may present acute lesions. Hemorrhages into the serous membranes are often met with, and the organs in general show degenerative changes due to action of the toxins. Endocarditis is rarely seen. Catarrhal bronchitis and bronchopneumonia frequently complicate diphtheria, and are caused by the inspiration of pyogenic cocci as well as by the invasion of the Klebs-Löffler bacillus itself.

SYMPTOMS.—The symptoms of diphtheria vary much in severity, and also vary with the locality attacked. The following types will be described: (1) *The Typical form* or general disease picture. (2) *The Mild form*. (3) *The Severe form*, or malignant diphtheria. (4) *Nasal diphtheria*. (5) *Laryngeal diphtheria*. (6) *Special localizations*.

THE TYPICAL FORM

The prodromal symptoms of diphtheria are not especially typical. They may be acute in character, or very mild and of a subacute variety. In young children there may be at the onset of the disease a slight convulsion. In certain cases, a peculiar dark-red appearance of the mucous membrane of the mouth is seen, which is quite characteristic. There is apt to be a sensation of chilliness, some heightening of the temperature, and more or less pain in the back and limbs. There is nothing, however, to distinguish this stage from many other affections of children, such as simple tonsillitis. The child may often complain of discomfort on swallowing, and on examining the throat the fauces are found to be reddened.

In from twelve to twenty-four hours, however, a more typical appearance will be seen in the throat. A white or greyish-white

pseudo-membrane, commonly appearing first on the tonsils, develops, and on the second or third day extends to the soft palate and uvula. It may also extend backward to the pharynx. During this stage the throat becomes much swollen and the tonsils considerably enlarged, so as almost to meet at times in the median line. The diphtheritic membrane is usually firmly adherent to the mucous membrane, and, as the case progresses, assumes a brownish or yellowish-grey color, sometimes becoming gangrenous, with an extremely fetid odor. A profuse nasal discharge may appear at this stage. Listlessness is present, but delirium of an active type is not common. In addition to these lesions in the throat, the cervical glands are usually involved and become considerably swollen.

The child, as a rule, shows grave constitutional symptoms. The temperature is not characteristic. It is usually not especially high, and ranges from 101° to 102° F. It may, however, rise to 104° F. A subnormal temperature is more serious than a moderately elevated one. The pulse is increased in rapidity, and is weak in proportion to the severity of the disease, but does not always correspond to the temperature; sometimes it is very slow. The slow pulse is indicative of the action of the toxin on the nervous centers, as well as of the weakness of the myocardium. Diarrhea is a frequent but not a constant symptom. Loss of appetite, nausea, and vomiting frequently occur.

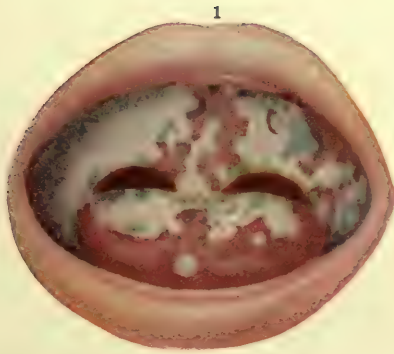
In typical cases the symptoms abate towards the end of the first week, the pseudo-membrane separates, leaving a raw surface behind, the neck becomes less swollen, and the child feels much better. It is, however, usually left in a prostrated condition for a number of weeks; and even in these comparatively mild cases the toxic effects of the disease may show themselves in the form of a neuritis with an accompanying paralysis many weeks after the diphtheria has run its course. There may also, even in mild cases, be a slight discharge from the nose, owing to the inflammation of the posterior nares. Slight albuminuria is not infrequent.

A very prominent symptom in all forms of diphtheria may be cardiac weakness. In some cases the child dies suddenly without any warning, or death may be preceded by attacks of semi-collapse. In other cases there may be a weak intermittent pulse, which continues throughout the disease and during convalescence. Under these circumstances the child should be considered to be in a critical condition, as death is likely to occur suddenly.

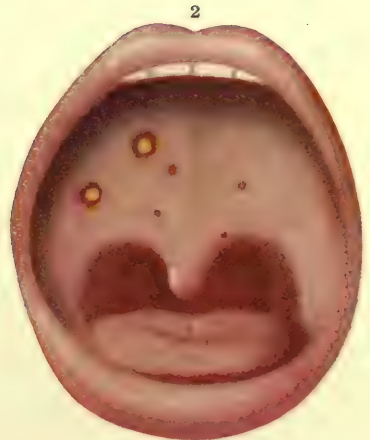
THE MILD FORM

A great number of cases, especially in older children, are of a very mild type. These cases are accompanied by very slight constitutional disturbance. The temperature is moderately raised, 100° F.

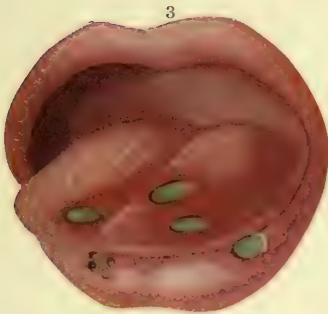
PLATE XII.



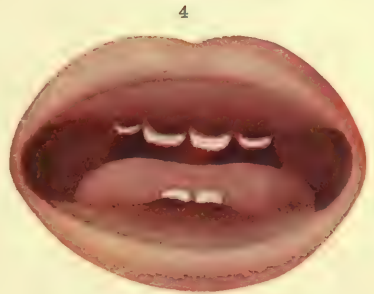
Thrush.



Varicella.



Stomatitis herpetica.
Aphthosa.)



Stomatitis ulcerosa
(Scorbutus.)



Follicular tonsillitis



Diphtheria.

to 101° F., and there are few other symptoms except slight apathy, loss of appetite, and slight sore throat. The membrane is confined to the tonsils, does not spread, and disappears in from three to five days. The enlargement of the cervical lymphnodes is only moderate.

Some cases are still milder. No typical membrane is seen. The tonsils are little inflamed, and in their crypts are seen greyish-white spots about the size of the head of a pin, or a little larger. The appearance closely resembles follicular tonsillitis, but the areas really consist of bits of membrane which are more adherent than the exudate in tonsillitis, and contain diphtheria bacilli. Sometimes these bits of membrane later coalesce into typical membrane, or the diagnosis may be clinically confirmed by the appearance of laryngeal stenosis, or by the later appearance of paralysis.

There is a still milder form, which is often called catarrhal diphtheria. In these cases no membrane or exudate appears, and the throat presents the appearance of an ordinary catarrhal angina, with moderate redness, swelling and increased secretion of mucus. These cases can transmit the bacillus to others, and in more susceptible individuals a severe form may be produced. A purely clinical diagnosis in such cases is impossible, and at most diphtheria can only be suspected from the presence of the disease in the family, house, or neighborhood. The diagnosis can only be made by culture and bacteriological examination.

THE SEVERE FORM—MALIGNANT DIPHTHERIA

In addition to these mild cases, the Klebs-Löffler bacillus at times produces a most severe form of diphtheria. In these cases the child either shows a fairly mild form of the disease for a few days and then suddenly develops the severe form, or it may be attacked at once by very severe symptoms. It becomes dull and markedly prostrated; the temperature is either slightly raised or may rise to 103° or 104° F. or higher; vomiting and headache may be present; the pseudo-membrane spreads rapidly. There may be a dusky efflorescence on the skin, simulating closely that which has been described in the malignant form of scarlet fever. There may also be a purpuric condition of the skin. The tonsils and throat are markedly swollen. The picture of these septic cases is very characteristic. There is a peculiar sweetish odor to the breath. There is cyanosis and a marked waxy pallor. There are hemorrhages from the throat and nose, with a profuse muco-purulent discharge from the latter. The cervical glands are often enormously enlarged. The breathing becomes difficult from the extension of the membrane in the pharynx, and from the swelling of the tonsils and pharyngeal tissue, and nasal breathing may be impossible. Swallowing is very difficult, and the speech is thick. The membrane has been known to extend in all directions, and some-

times even through the Eustachian tubes to the ears. All degrees of severity are met with between the mild and malignant types of diphtheria. The membrane, instead of extending upward to the nasopharynx, as occurs in the malignant cases just spoken of, may spread downward, attacking the epiglottis and the larynx, and cause serious obstruction.

The general condition is much affected. The children lie in apathy, with open, staring eyes. Occasionally they toss about in bed. There is complete loss of appetite. Although thirsty, it is difficult to get them to take any fluid. The fever may be high and remittent, or only slightly raised. The pulse is rapid, of small volume, and very easily compressible; it may be thready and hardly palpable. The extremities become cold and cyanotic.

The heart sounds are feeble. There may be a systolic murmur at the apex. Later, dilatation with enlargement of the liver, may occur. The spleen is somewhat enlarged, but may not be palpable. The urine contains albumin and casts.

In some severe forms the symptoms may be partly due to an associated streptococcus infection of the throat, which may spread as in scarlet fever. Such types have been described as "septic diphtheria." The streptococcus, however, may be present without playing much part, the severity of the symptoms being due to the diphtheria infection. The term "malignant diphtheria" is preferable.

The course of severe diphtheria has been much modified by serum therapy. Before the days of antitoxin, the majority of these severe cases died in the second half of the first week, either from intoxication and circulatory failure, or from bronchopneumonia. With early serum treatment, the severe progress of the case can often be arrested in time. In such cases the throat becomes clear of membrane by the end of the first week. Convalescence is, however, slow, taking a number of weeks, and there remains still the possibility of a sudden death from heart failure.

NASAL DIPHTHERIA

Diphtheria sometimes begins in the nose and spreads no farther. Primary nasal diphtheria may be either very mild or very severe, according to where the membrane is situated. If the membrane forms in the anterior nares, the probability of absorption is reduced to a minimum, and there is usually very little constitutional disturbance. The condition is especially liable to be overlooked, as the child for one or two days may show merely the symptoms of fever, malaise, loss of appetite, and a discharge from the nose. On examining the nose carefully, however, a pseudo-membrane will often be found. It is, therefore, very important in cases of this kind to have a bacteriological examination made, and to isolate the child until it is

determined that the Klebs-Löffler bacillus is not present. These cases are a prolific source of infection to the community at large, for even when antitoxin has been given it does not immediately kill the bacilli, although it may stop the nasal discharge.

The importance of recognizing nasal diphtheria of this type lies in preventing the spreading of the disease to others. The history of many serious outbreaks of diphtheria is due to the fact that some member of a family or some inmate of an institution has had a profuse discharge from the nose without any constitutional disturbance, and has been the focus from which has arisen many severe cases of diphtheria. This is not a theoretical statement, but is the result of experience. Every profuse discharge from the nose, particularly if there is any excoriation about the nostrils, should be looked upon with suspicion and cultures should be taken. A unilateral discharge is always suspicious, usually meaning either diphtheria or a foreign body. If adenoids are to be removed, cultures should always be taken before the operation is performed, for it very frequently happens that a child who has had a profuse discharge from the nose, has a severe attack of diphtheria, immediately after the removal of the adenoids or the excision of the tonsils. If the operation for cleft palate is to be performed, it is still more important to take cultures; because, if there are any bacilli of diphtheria in the nasal discharge, this organism is sure to grow upon the surfaces of the operative tract, and the patient not only has an attack of diphtheria, which may be mild or severe, but also the edges of the wound slough and render a second operation much more difficult.

When the disease is situated in the posterior nares and the nasopharynx is affected, either primarily or secondarily through the nares or the pharynx, the constitutional symptoms are, as a rule, marked. This is in all probability accounted for by the great mass of lymphatics in the nasopharynx, where absorption takes place so easily that general septic poisoning quickly follows, often with fatal result. In these cases the toxin generated is very readily absorbed and may cause death from its effects on the heart. Many patients die from unrecognized nasal diphtheria, because no membrane is seen, and the first indication of serious trouble is a rapid action of the heart known as the *bruit de galop*, or, in some instances, there may be a slow pulse, and the physician is often unable, if he does not have the idea of nasal diphtheria in mind, to explain the symptoms.

LARYNGEAL DIPHTHERIA

This form of diphtheria is what is commonly known as "*true croup*," or "*membranous croup*." It includes all cases in which the membrane extends into the larynx, trachea, and bronchi. It is the most dreaded of all the clinical forms of diphtheria. It is most

common in infants and younger children, its frequency bearing an inverse proportion to the age.

Extension of the diphtheritic process to the larynx can occur in the course of diphtheria of the nose, tonsils or pharynx. The involvement of the larynx may occur simultaneously with the process in the throat, or may develop later, in three to seven days. It may occur in the course of a mild catarrhal faucial or nasal diphtheria, in which no membrane has been observed. In these cases cultures from the nose and throat are positive for Klebs-Löffler bacilli.

It is important to remember, however, that in young children *the larynx may be the primary site of the diphtheritic process*, and may be severely involved, while the nose and throat remain entirely free. In such cases cultures from the nose and throat may be negative.

The first symptoms of laryngeal diphtheria are *hoarseness* and *cough*. The chief symptom is *increasing inspiratory dyspnea*.

The hoarseness increases until complete aphonia is present. The cough is at first of a harsh ringing character, but later becomes husky and painful.

Either at the beginning in very young children, or a little later in older children, inspiration becomes prolonged and noisy. It resembles the breathing in an attack of common or false croup, but becomes steadily worse, is uninfluenced by the ordinary treatment of common croup, and does not improve by day.

Steady progress, steadily increasing severity of symptoms, is characteristic of laryngeal diphtheria. There is, however, the greatest variation in the rate of progress. The full development of the picture may be reached in twenty-four hours, or may not be reached for four or five days. The inspiratory obstruction becomes dyspnea, and this becomes more and more marked. If the lungs are clear, the rate of respiration is not increased, but the noisy and prolonged inspirations cause marked effort, and are accompanied by retraction of the intercostal and supraclavicular spaces, and later of the epigastrium and lower chest. These signs become more and more marked, and finally *increasing cyanosis develops*.

The temperature may or may not be raised. As the toxic absorption is slight, on account of the locality affected, the constitutional symptoms are correspondingly mild. The child is very restless, is forced to sit up in order to breathe, and, for the same reason, bends its body forward with its head back.

Inspection of the throat shows signs which vary according to whether the laryngeal process is primary, or secondary to a primary process in the throat. There may be membrane visible in the throat, or only redness and swelling of the tonsils and mucous membrane, or there may be nothing abnormal seen. If a tongue depressor be placed on the back of the tongue, and strong pressure made, the

reddened and swollen epiglottis can often be seen, and sometimes a bit of membrane. Laryngoscopic examination would of course show the membrane in the larynx, but this is rarely practicable in children.

The labored, obstructed breathing and cyanosis grow worse, if no treatment is instituted. The face and hands become bathed in cold sweat, and the child's restlessness gives place to somnolence. Sometimes spontaneous improvement occurs, and this may be brought about by the child expelling some membrane in coughing. Without treatment, the usual ending is death from asphyxia.

SPECIAL LOCALIZATIONS

The Mouth.—Diphtheria of the mouth is rare, and is almost always secondary to diphtheria of the throat. There is typical membrane formation, usually on the cheeks and lips rather than on the tongue.

The Conjunctiva.—Diphtheria of the conjunctiva is not extremely rare, and is often primary. In mild cases there is a thin membrane on the palpebral conjunctiva, with swelling and redness of the lids, and purulent secretion. This form may recover without further damage. In more severe cases the membrane is more adherent, and the swelling and inflammation is much greater. This may result in destruction of the cornea.

The Skin.—Diphtheria of the skin is seen at times, when there is a wound or lesion. It is usually secondary to a process in the throat, but may be primary. The membrane is often thin and hardly visible.

The Vulva.—Diphtheria of the vulva is rare. It is usually secondary, the infection being carried from the mouth by the fingers. Any inflammatory condition of the vulva favors infection. There is a marked phlegmonous inflammation with a thick membrane, and the affection runs a severe course, sometimes leading to gangrene.

COMPLICATIONS AND SEQUELAE.—The principal complications and sequelae of diphtheria involve *the lungs, the heart, the ears, the kidneys and the nervous system.*

THE LUNGS.—Severe bronchitis and bronchopneumonia are frequent complications of diphtheria. Bronchopneumonia is often seen not only in laryngeal diphtheria with membrane extending into the trachea and large bronchi, but also in the severer cases of faucial diphtheria. The clinical type shows the characteristics of a secondary bronchopneumonia, with nothing characteristic of, or peculiar to, diphtheria. The diphtheria bacilli may be found in the areas of consolidation, but the process is due to a mixed infection, the commonest bacteriological finding being numerous streptococci. It is probable that the diphtheria acts as a predisposing cause. Bronchopneumonia is a frequent cause of death in severe cases of diphtheria, particularly in cases of laryngeal diphtheria which die in spite of intubation or tracheotomy.

THE HEART.—The toxin of diphtheria always affects the heart, signs of cardiac weakness having already been mentioned as characteristic of diphtheria, so that they constitute a symptom rather than a complication. The severity of the cardiac weakness is in proportion to the severity of the case. The weak pulse, dilatation and murmur have already been described. Cardiac weakness is the commonest cause of death in the malignant type. The blood pressure observations are not very reliable in children. The circulatory disturbance is probably more vasomotor than cardiac.

There is sometimes seen in diphtheria a peculiar form of heart failure which is characteristic of the disease and which causes *sudden death*, the "*Tierstod*" of the German writers. Sudden cardiac failure may occur during the height of the disease. It is often preceded by malaise, pallor, abdominal pain, and a weak irregular pulse, but these symptoms are not severe enough to suggest so sudden a fatal ending.

More characteristic of diphtheria is the so-called post-diphtheritic heart failure, which occurs after the disease has subsided, in the fourth, fifth, or occasionally even as late as the eighth week. It is most often seen after severe cases, but occasionally occurs after typical or even mild cases. The children usually show marked prostration after the disease has subsided, and remain weak, and pale. The pulse remains rapid and irregular, but is sometimes slow at times—a still more dangerous sign. Every slight exertion greatly increases the frequency of the pulse. Occasionally there are attacks of weakness, sudden pallor, dyspnea, vomiting, or abdominal pain. These premonitory symptoms can go no farther, and can be recovered from in the course of one or two months. At times, however, after the child is believed to be wholly out of danger, sudden death may occur. The cause is believed to be either a myocarditis of toxic origin, or more commonly, a toxic degeneration of the nervous mechanism governing the heart.

THE EAR.—Otitis media is a frequent complication of diphtheria. In most cases it is not due to the Klebs-Löffler bacillus, but to a mixed infection, as in any infectious disease involving the throat. Secondary diphtheria of the ear, caused by the excursion of the specific organism from the throat to the nasal passages, and thence to the ear, through the Eustachian tube, can occur. Improper methods of treatment, such as unwise irrigation, increase the danger of ear complications.

THE KIDNEYS.—In most cases of diphtheria albuminuria is present, with numerous casts. This represents a degeneration of the epithelium of the convoluted tubules. A severe nephritis involving the glomeruli, with diminished urine and edema, is rare.

THE NERVOUS SYSTEM; POST-DIPHTHERITIC PARALYSIS.—This is the most important sequela of diphtheria. The toxin of diphtheria has an especial affinity for the nervous system, resulting in peripheral nerve paralysis. This is a late manifestation of the disease, and appears at a time when the ordinary toxic manifestations of diphtheria are over, usually in the second, third, or fourth week. It is a question whether this manifestation is due to the same poison as produces the other symptoms, or whether there are not more than one poison, paralysis being due to the "toxone" as suggested by Ehrlich. The anatomical basis for the paralysis is a peripheral nerve degeneration. The fact that cases have been observed in which there was membrane on only one side of the throat, and in which a unilateral paralysis of the palate occurred, and that in diphtheria of the skin the nearest muscles are most apt to be paralyzed, suggests that the poison reaches the central nervous system along the course of the nerves rather than through the blood.

The commonest type of post-diphtheritic paralysis involves the muscles of the soft palate. The symptoms are a *nasal voice*, and the fact that the *taking of fluid causes cough* and the *regurgitation of part of the fluid through the nose*. Inspection shows that the soft palate and pillars hang limp, and do not move with gagging, phonation, or inspiration. The paralysis may be unilateral. The palatal reflex is absent. Sometimes the muscles of deglutition are involved, so that swallowing is difficult or impossible. In palatal paralysis recovery occurs gradually in from two to four weeks.

Next in frequency to paralysis of the palate is paralysis of accommodation of the eye. This is often overlooked in young children, but if careful observation is employed, it will be noted that the fixing of the eyes on a finger or object held near the face is either not so complete, or not so prompt as it should be. Older children complain of inability to read and write. At times, in addition to paralysis of accommodation, there is paralysis of other muscles of the eye, which causes strabismus or double vision.

Besides these two most common types of post-diphtheritic paralysis, in rarer cases any of the other groups of muscles all over the body may be involved. In the lower extremities weakness or ataxia is commoner than actual paralysis. The muscles of the neck are sometimes involved. Very rarely is there paralysis of the back, face or larynx. Paralysis of all the muscles of the body has been observed. Paralysis of the diaphragm, or of other muscles of respiration may be dangerous to life.

Disturbances of sensation are very uncommon. In severe cases there may be incontinence of urine and feces.

In most cases of diphtheritic paralysis, although there may be no involvement of the lower extremities, there is *disappearance of*

the *patellar reflex*, which lasts a number of weeks, and is sometimes permanent. The electrical reaction of the paralyzed muscles shows a mild reaction of degeneration.

DIAGNOSIS OF DIPHTHERIA. BACTERIOLOGICAL DIAGNOSIS.—The positive diagnosis of diphtheria depends upon the finding of the Klebs-Löffler bacillus in the lesions present. Bacteriological examination should be made in every suspicious case. Although faucial diphtheria can often be recognized clinically with a fair degree of certainty, there is always some doubt without bacteriological proof, and the most typical-looking membrane may not be diphtheritic. So important is the early recognition of diphtheria, that I believe that a bacteriological examination should be made in every case with sore throat, or with any lesion or acute inflammation involving the throat. It should also be made in cases with nasal discharge and constitutional symptoms, or with unilateral or bloody nasal discharge.

The bacteriological examination may be made both by means of *cultures*, and of *fresh cover-glass preparations*. The results of cultures are more certain, but they require more time. I believe that both methods should be employed.

The material both for cultures and for fresh cover-glass preparations is obtained in the same way, by means of a small sterile cotton swab. This should be preferably rubbed at the edges or under the edges of the membrane rather than upon the surface. If typical membrane be not present, the swab should be rubbed upon any spots which may appear in the crypts of the tonsils, or if there be no spots, upon any part of the mucous membrane which appears most inflamed. If there is a suspicion of laryngeal diphtheria, the swab should be applied to the posterior wall of the pharynx. Two swabblings should be taken, one of which is rubbed upon the surface of Löffler's blood-serum culture medium, and the other upon the surface of the cover-glass. The culture should be incubated for twelve hours, and then cover-glass preparations are made from the surface of the medium. The fresh cover-glass preparation may be examined at once. The cover-glasses are dried, fixed, and stained with Löffler's methylene-blue. The diphtheria bacilli are recognized by their comparatively large size, by their irregular staining, and by their tendency to occur in clumps. In cases with any clinical symptoms, it is better for purposes of treatment to regard all microorganisms having a characteristic appearance as true diphtheria bacilli, although the pseudo-diphtheria bacillus cannot be excluded with certainty. In cases where it is a question of a carrier, it is best if possible to differentiate the true from the pseudo type. This can only be done by means of animal inoculation.

DIFFERENTIAL DIAGNOSIS OF FAUCIAL DIPHTHERIA.—While the

diagnosis of faucial diphtheria depends mainly upon the bacteriological examination, it is necessary that the physician be familiar with those conditions which bear the closest clinical resemblance to diphtheria. Among these are *catarrhal pharyngitis*, *follicular tonsillitis*, *membranous angina*, *Vincent's angina*, and atypical appearances in various *other forms of angina and stomatitis*.

A simple *catarrhal sore throat*, showing no membrane or exudate, is not clinically suggestive of diphtheria, and most cases of this type are not diphtheritic. Nevertheless, infection with the diphtheria bacillus may produce only a simple catarrhal inflammation, and such cases can only be recognized by bacteriological examination. It is for this reason that I recommend the taking of cultures from all cases of sore throat.

Diphtheria may show only bits of membrane in the crypts of the tonsils, resembling the appearance of *follicular tonsillitis*. On the other hand, in follicular tonsillitis the exudate in the crypts may increase in amount, and the areas may coalesce, so that all or a large portion of the tonsil may be covered, resembling the appearance of diphtheria. In follicular tonsillitis high fever is much more constantly present than in diphtheria. Moreover the exudate in tonsillitis is usually yellowish, sticky, purulent, and foul-smelling, and is more easily wiped off than is the membrane of diphtheria, which is whiter, tougher, and more adherent. Most cases with discrete spots in the crypts of the tonsils are tonsillitis, but the differential diagnosis can only be made with certainty by bacteriological examination.

A membranous lesion of the tonsils is not always diphtheria. It occurs frequently in scarlet fever, and occasionally from other causes. The *scarlet fever angina* is recognized by the other features of the disease, but bacteriological examination is essential in every case of membranous angina.

Vincent's angina may bear a close resemblance to the lesion of diphtheria. It usually involves only one tonsil, and may often be recognized by the fact that destruction of tonsillar substance and ulceration begin early. In diphtheria the membrane appears to be plastered over the surface of the tonsil, while in Vincent's angina it often appears to fill a large ragged crater. The inflammatory reaction of the tissues around the lesion is much less in Vincent's angina than in diphtheria. The gangrenous odor from Vincent's angina is often marked enough to be characteristic. Constitutional disturbance is less marked in Vincent's angina than in diphtheria. While all these points may enable the physician to make a probable clinical diagnosis, certainty can only be attained by bacteriological examination. In Vincent's angina fresh cover-glass preparations are characteristic, showing the bacillus fusiformis with its associated spirochetæ.

In certain cases atypical forms of thrush, stomatitis herpetica, syphilis of the mouth or throat, and Bednar's aphthae may be mistaken for diphtheria. Bacteriological examination will settle such doubtful questions.

DIFFERENTIAL DIAGNOSIS OF LARYNGEAL DIPHTHERIA.—The diagnosis of laryngeal diphtheria in cases which have already shown the evidences of faucial or nasal diphtheria, is not difficult. The signs of laryngeal obstruction, hoarseness, harsh cough, and increasing inspiratory dyspnea are easily recognized, and in these cases their connection with the diphtheria infection already present is obvious.

Difficulty is encountered in the cases, not uncommon, in which the laryngeal process is the primary manifestation of the disease. The clinical diagnosis mainly depends on the *steadily increasing* signs of laryngeal obstruction. Bacteriological examination of material taken from the pharynx often shows the presence of diphtheria bacilli, particularly in cultures. On the other hand, the results of cultures cannot be used in excluding laryngeal diphtheria, as the cultures are often negative. Consequently, the clinical diagnosis is more important than in faucial diphtheria.

The conditions to be considered in differential diagnosis are all which may cause obstructive dyspnea. The most important are *acute laryngitis (spasmodic croup, common or false croup)*, *retropharyngeal abscess*, and *foreign body in the larynx*. Occasionally the dyspnea from thymic enlargement, or pressure from enlarged bronchial lymphnodes, has led to a suspicion of laryngeal diphtheria, but the diagnosis is usually clear from a careful history of the case. Papilloma of the larynx produces symptoms which come on so much more gradually, that it is rarely confused with laryngeal diphtheria.

In *spasmodic croup*, the attack is sudden, usually occurs at night, and is spasmodic in character. The voice is almost never lost. The attack usually remits, and obstructive dyspnea disappears the next morning. Rarely some dyspnea may persist on the day following the attack, but it is well to treat any such case as diphtheria. The history of previous attacks points toward spasmodic croup.

In the severe form of *acute catarrhal laryngitis*, with dyspnea, but without spasm, the diagnosis may be more difficult, especially in the first twelve hours. Laryngoscopic examination will often clearly differentiate the two conditions, but it is neither practicable nor conclusive in infants. The dyspnea in catarrhal laryngitis is more likely to be paroxysmal and remittent, and is mainly inspiratory, while in laryngeal diphtheria it is both inspiratory and expiratory, and increases steadily. The voice is usually not lost in catarrhal laryngitis, and the temperature is usually higher than in diphtheria. In cases in which any doubt exists, it is best to give antitoxin at once.

In *retropharyngeal abscess* there is increasing obstructive dyspnea, and the extension of the inflammation of the mucous membrane to the larynx often causes hoarseness and cough. There is not usually loss of voice in retropharyngeal abscess, and the dyspnea is of a somewhat different character, often accompanied by a peculiar sound on expiration, and with inspiration proportionately less labored. The diagnosis depends on the results of careful examination of the pharynx, both by inspection and by exploration with the finger.

I have mistaken *foreign body* in the larynx for laryngeal diphtheria. Usually with foreign body the onset of obstructive symptoms is sudden, not preceded by hoarseness and cough. The history is often of aid. Occasionally, however, the foreign body does not at once produce marked obstruction, but causes an inflammation which leads to an increasing severity of symptoms. In such cases, with an unsatisfactory history as to the disappearance of any plaything or other object, the diagnosis is difficult, and can only be made by laryngoscopic examination.

DIAGNOSIS OF NASAL DIPHTHERIA.—The taking of cultures from every case with nasal discharge would be required in order to be sure of the recognition of every case of nasal diphtheria. This, while theoretically desirable, would involve so much labor, on account of the frequency of catarrhal rhinitis, that it will probably never be carried out. I would advise, however, that cultures be taken in all cases with *unilateral discharge, blood stained discharge, or unduly persistent discharge*.

DIAGNOSIS OF POST-DIPHTHERITIC PARALYSIS.—This condition is usually so characteristic, that even in cases with a defective previous history, or in which the diphtheria was of so mild a type as to have been overlooked, the recognition of the diphtheritic origin of the paralysis is usually easy.

PROGNOSIS.—Diphtheria is an extremely fatal disease, especially the septic and obstructive cases. The mortality varies decidedly in different epidemics and according to the age. It is greatest in children under two years of age, but has been lessened in cases in which the antitoxin treatment has been thoroughly used. In the acute stage, death may occur either from laryngeal stenosis, bronchopneumonia, or by the effect of toxin generated from the growth of the bacillus. In the later stages or during convalescence it may be due to the action of the toxin on the nervous centers. The symptoms which make the prognosis especially unfavorable are the extension of the membrane to the naso-pharynx or the larynx, profuse nasal discharge, marked septic odor, extensive glandular enlargement, hemorrhage from the nose or into the skin, a high grade of albuminuria, bronchopneumonia, and a weak heart. In cases of post-

diphtheritic paralysis the prognosis is good, as they almost invariably recover. The prognosis in all cases of diphtheria is uncertain and should be given with caution, and no case of diphtheria should be considered benign, for at times in certain mild cases serious symptoms may arise, and death from heart failure is liable to occur at any stage of the disease. A child who has had diphtheria is liable to suffer from the deleterious effects of the disease for months and even years. Before antitoxin was used, the mortality from diphtheria in the Boston City Hospital was 50 per cent. Since its use in a series of 4500 cases in the diphtheria wards of the Boston City Hospital the mortality has been reduced to 13 per cent., and if the moribund cases, which numbered 179, by which are meant those dying within twenty-four hours after admission to the hospital, are deducted the mortality was about 10 per cent.

PROPHYLAXIS.—As diphtheria is a disease having the same degree of contagiousness and the same mode of transmission as scarlet fever, the measures of isolation, quarantine, and disinfection employed in preventing the spread of the disease are much the same. The diphtheria patient should be isolated, with the nurse, and a most rigid quarantine should be established, the arrangement and management of the sick room being the same as for scarlet fever. Whenever such strict isolation and quarantine cannot be obtained in a private house, the patient should be sent to a diphtheria hospital. The quarantine must be very rigidly enforced in the case of the nurse who cares for a diphtheria patient, on account of the fact that a healthy person may become a carrier of virulent Klebs-Löffler bacilli. The nurse of a diphtheria patient should come in contact with no other person. Similarly, no member of the patient's family, and no other person, should be allowed within the quarantined quarters, unless such person is prepared to submit to permanent quarantine with the patient.

The only exception is the physician, who must visit the patient from time to time. He should take the most rigid precautions against a possible contamination of his person with infected material, wearing gown, cap and gloves as described for scarlet fever, and being most thorough in cleansing his hands and face after each visit. I further believe that every physician caring for a case of diphtheria should take frequent cultures from his own throat, in order to make sure that he has not become a carrier.

The other children in the family in which a case of diphtheria has occurred, should be kept out of school, and should not be allowed to play with other children. Cultures should be taken from the throats of every member of the household, and of every person who has been exposed. This is important in detecting mild incipient

cases of diphtheria as well as carriers. All persons in whom a positive culture is obtained should be placed under quarantine.

Not only should every undoubted case of diphtheria be immediately isolated, but also every suspected case. It is my practice to isolate every case of sore throat occurring among the children under my care, until the results of cultures for diphtheria, and the expiration of the prodromal period of scarlet fever, have demonstrated that neither of those diseases is present. In an epidemic of diphtheria every sore throat and nasal discharge is particularly suspicious, and the child should be isolated until the results of the cultures are known. While such extreme watchfulness is generally only recommended in institutions, I believe that it is equally important in private families. It should be remembered, however, that cases isolated on suspicion only of a contagious disease, should be kept by themselves and not exposed to possible infection from other cases, until it is certain that they actually have the disease. In cases in which the clinical manifestations are strongly suggestive of diphtheria, in times of epidemic, and in persons who have been actually exposed, the negative result of a single culture should not be accepted as conclusive, but several, at least three, should be taken before quarantine is relaxed.

The immunization by giving antitoxin of individuals who have been exposed to diphtheria will prevent the development of the disease. It does not, however, prevent an individual from being a carrier, and should not be allowed to take the place of the taking of cultures from the noses and throats of such persons. Until recently the immunization of every person exposed has been recommended. Since it has been shown that many children have a natural immunity, which can be demonstrated, it is not necessary to immunize a child who has a negative Schick reaction. *Every exposed child, however, who has a positive Schick reaction, or on whom the Schick reaction is not performed, should receive an immunization dose of antitoxin.* The quantity of antitoxin which has usually been recommended for immunizing purposes is 500 units for infants, and 1000 to 1500 units for older children. Recently numerous writers have been recommending the proportioning of both prophylactic and therapeutic doses of antitoxin to the body weight of the patient, which gives us a more definite procedure. For immunizing purposes Schick recommends 50 units per kilogram of body weight.

In hospitals devoted to the care of children, the practice of periodic immunization of all patients admitted to the hospital has proved highly successful. At the Children's Hospital, Boston, from May 1, 1897 to October 1, 1905, 10,575 patients were treated, and at the Infant's Hospital, from February 1, 1900, to October 1, 1905, 1276 cases were treated. During these years, under prophylactic immuniza-

tion, no case of diphtheria broke out in the wards. At present at the Infant's Hospital a routine Schick reaction is performed on every case, and only those not having natural immunity receive antitoxin.

The length of time during which quarantine should be continued depends on the results of bacteriological examination. The patient must not be released until the bacilli have disappeared from the mucous membrane. This time is very variable. In about half the cases the organisms disappear within three days after the membrane is gone, while in the great majority of the remaining cases they disappear within a week. In certain individual cases they may persist for a much longer, indefinite period, which may reach many weeks. The results of a single culture should not be taken as conclusive. The Boston Health Board requires three successive negative cultures, which I believe to be a wise rule. Cultures should be taken from both the throat and the nose.

Many cases in which the bacilli persist for a long time are instances of nasal diphtheria. It has been shown that in many of these cases the bacilli are non-virulent. In healthy persons in whom positive cultures are obtained, the bacilli may also be non-virulent. It has been questioned whether the isolation of healthy carriers, and of cases of nasal diphtheria with continued positive cultures, is desirable or necessary. It has also been shown that in many of these cases of nasal diphtheria or of healthy carriers the bacilli are very virulent. Therefore it is better to isolate all such cases unless the bacilli are shown to be non-virulent by animal experimentation.

The measures which are employed in diphtheria in the disinfection of clothing and utensils, are the same as those described for scarlet fever. Also the measures which are taken upon the release of a child from quarantine, and in the subsequent disinfection of the sick room, are in no way different from those used in scarlet fever, and have already been fully described.

TREATMENT. SERUM THERAPY.—It is in diphtheria that serum therapy has won its greatest triumph, and for this reason the antitoxin treatment of diphtheria must first be considered. The immune body through which recovery from diphtheria occurs is an antitoxin, which acts by neutralizing the toxin which causes the injurious effects of the disease. The serum of horses which have been treated with repeated injections of a filtrate from cultures of the Klebs-Löffler bacillus, contains a large quantity of this immune body. The antitoxic power of such serum is measurable, as the neutralizing action of the immune body is as definite as a chemical reaction. The unit of measure is the amount of antitoxin which will protect a guinea-pig weighing 250 to 300 grammes against one hundred times the fatal dose of diphtheria toxin. Behring's original serum contained this

amount in one c.c. of horse serum, but improvements in the method of preparation have permitted a much greater degree of concentration of the serum, so that many units are contained in one c.c. In using the serum, the physician must know the number of antitoxin units to the cubic centimeter in the particular serum employed. Only serum prepared by a reliable manufacturer should be used. When kept properly in a cold, dark place, preferably upon ice, serum will retain its full antitoxic properties for a considerable time. If, however, the serum is more than six months old, it is better if possible to obtain a fresh preparation.

While the chief result of the injection of immune serum in diphtheria is the neutralizing of the toxin, there is also evidence of some injurious action upon the bacilli themselves, the nature of which is as yet imperfectly understood. On account of the nature of the immune body, the serum used in the treatment of diphtheria is generally called *antitoxin*. This is not strictly correct; the antitoxin is the principal immune body contained in the serum.

Indications for Serum Therapy.—While the beneficial results of the serum treatment of diphtheria are now generally recognized, there are some authorities who, on account of the untoward effects which sometimes follow the administration of antitoxin, advocate that it be not used in certain mild cases in older children. I do not agree with this opinion. One can never know beforehand that a case of diphtheria will continue to be mild throughout its course, as severe symptoms may appear unexpectedly at any time. Furthermore the advantages of an early administration of antitoxin are very great. I believe, therefore, that serum therapy should be employed in every case. The question does arise as to whether antitoxin should be given to suspected cases immediately, and before the bacteriological investigation has confirmed the diagnosis. This depends on the severity of the case, and the amount and character of the clinical evidence pointing toward diphtheria. I would summarize the indications for serum therapy as follows:

1. In all cases proved to be diphtheria by positive bacteriological investigation.
2. In cases in which, before the bacteriological examination is completed, membrane is seen.
3. In cases in which the patient, while not having typical membrane, shows appearances in the throat compatible with diphtheria, and marked constitutional disturbance, or any dangerous and threatening symptoms, while the physician is waiting for the results of the cultures.
4. In cases which have developed any signs of laryngeal obstruction which cannot definitely and certainly be attributed to some other cause.

The dose of diphtheria antitoxin.—This varies greatly with the age of the child, with the situation of the lesion, and with the severity of the case. The initial dosage may be summarized as follows:

1. In mild cases of diphtheria involving the throat or nose alone, 3,000 to 5,000 units.
2. In cases of average severity, involving the throat alone, 5,000 to 7,000 units.
3. In severe cases of faucial diphtheria, cases involving both the throat and the nose, and average cases of laryngeal diphtheria, 7,000 to 10,000 units.
4. In malignant diphtheria and severe cases of laryngeal diphtheria, 10,000 to 15,000 units.

In each group enumerated above, the lower figures apply to younger children, and the higher figures to older children.

Schick has recently done some experimental work on the dosage of diphtheria antitoxin, measuring the results by the effect upon his cutaneous reaction. He recommends the following dosage:

1. In mild cases, 100 units per kilogram of body weight.
2. In severe cases, 500 units per kilogram of body weight.

The injection of serum should produce a noticeable and continued beneficial effect. If after eight hours such an effect is not seen, or if at any time this improvement ceases, the injection of antitoxin should be repeated.

The method of administering antitoxin serum in diphtheria.—The serum was formerly injected into the subcutaneous cellular tissue, the seat of the injection being of no particular importance. It has been shown that absorption from muscular tissue takes place much more rapidly than from the subcutaneous tissue, and that intramuscular injections are less painful. Consequently, *as a routine, intramuscular injections should be used.* The preferable points for the injection are either the muscles of the outer side of the thigh or the muscles of the gluteal region. The skin should be thoroughly cleansed with water and alcohol, and the needle and syringe should be boiled.

Animal experimentation has shown that the intravenous injection of antitoxin produces a much more rapid effect than intramuscular injection. The intravenous route has been more and more used of late, and the most favorable results have been reported. I believe that intravenous injection should be employed in all very severe cases, in which the serious condition of the patient demands a rapid effect. The ease with which intravenous medication can be used in infants, in whom the open fontanelle gives ready access to the longitudinal sinus, has led me to adopt the intravenous method of injection in all severe cases in infants.

The beneficial effects of serum therapy.—In diphtheria treated with antitoxin, the signs of the favorable action of the serum are unmis-

takeable. The temperature and pulse rate begin to fall within the next eight hours, and the general condition improves. During this period the membrane ceases to spread. In laryngeal cases the obstruction may increase for the next twenty-four hours, owing to the necrosis of epithelium injured before the injection, but after this time it diminishes. The favorable effect is further shown by the formation around the membrane of a distinct red line of demarcation, by the fact that the membrane shrinks, softens, rolls up at the edges, and finally after two or three days, loosens, and is cast off. The effect on the process in the nose is seen in cessation of the discharge. The swelling of the cervical lymphnodes diminishes. The membrane in the larynx and trachea loosens and is cast off rapidly, and frequent removal of the tube is sometimes required when intubation has been performed, to clear the larynx of detached membrane.

Value of early treatment.—The results of serum therapy in diphtheria depend very largely on the time of administration of the serum. The antitoxin can only prevent further damage, but cannot remedy damage already done to the tissues. The cells of the heart and nervous system are particularly susceptible to the deleterious action of the diphtheria toxin, and death is likely to occur at the height of the disease from cardiac failure, or from cardiac or respiratory paralysis. Damage sufficient to cause a fatal ending may occur in a variable period which may be very short, and this damage cannot be undone by the subsequent administration of antitoxin. Many severe cases are fatally injured before antitoxin is given, and the importance of early diagnosis and treatment cannot be overemphasized.

It must also be remembered that antitoxin is powerless against secondary streptococcus infection, such as phlegmonous inflammation of the throat or cellular tissue, bronchopneumonia and suppuration of the lymphnodes. It also does not prevent the occurrence of post-diphtheritic paralysis, which is not, however, a serious sequela.

Results of serum therapy in diphtheria.—The antitoxin treatment has since 1895 been so thoroughly tested all over the world, that it is no longer necessary to cite figures and statistics in support of its value. The percentage mortality in hospitals has been reduced to about a third of the previous figures. The mortality in all cities and countries where antitoxin has been used has been very strikingly reduced. There has been a striking reduction in the percentage of cases requiring operation for laryngeal stenosis, and in the mortality after tracheotomy or intubation.

The importance of early administration is emphasized by some statistics recently collected by Deycke, based on 78,028 cases.

TABLE 52

Mortality in Serum-treated Cases of Diphtheria, According to the Time of Injection

TIME OF INJECTION	MORTALITY
1st day.....	4.3%
2nd day.....	7.6%
3rd day.....	14.7%
4th day.....	19.7%
5th day.....	31.6%
6th day.....	31.3%
After 6th day.....	31.6%

Untoward effects of serum therapy; serum sickness.—When one injects into an animal organism the serum of a foreign species, there may occur a reaction which causes pathological symptoms. These are in no way due to the specific antibodies contained in the serum, and are seen in any form of serum therapy, but as horse serum is used more in diphtheria than in any other disease, these manifestations of serum reaction are best described in this place. The symptoms are not seen in every patient, but only in about 10 to 20 per cent, and appear to depend upon some constitutional peculiarity. Some individuals will always show a serum reaction, even when serum from different horses is used. On the other hand, the serum from a particular horse will sometimes produce a reaction in every patient, while the same patients do not react to the serum from another horse.

In susceptible individuals, there appears in the days after the injection of serum a swelling and sensitiveness to pressure of the lymphnodes which drain the site of the injection. This may persist two or three weeks. The commonest clinical manifestation is the *exanthem*, or *serum rash*, which belongs in the class of toxic erythemata. The serum rash appears usually from the seventh to the twelfth day after the injection. It begins ordinarily at the site of the injection, and may remain limited to this area, but more commonly spreads with an irregular distribution over the entire body. The commonest appearance is an urticaria-like erythema, with very large irregular areas. There may be smaller areas of erythema in between, with spots resembling those of measles. Scarlatiniform eruptions are also seen at times, but are rare, as are hemorrhagic lesions. Itching is usually severe. Fever may accompany a serum rash, and may last several days. Malaise and pain in the joints are seen at times. During serum sickness there is usually a pronounced diminution in the white blood count, the leukopenia being due to a drop in the number of polymorphonuclear cells. At times precipitins for horse serum can be demonstrated in the serum of the patient.

The diagnosis of a serum rash depends mainly on the history that horse serum has been injected. The itching, the irregularities in the character and distribution of the eruption, and the fact that

it never involves the mucous membrane of the mouth, are important points in differential diagnosis.

These serum rashes usually last for two or three days, but are rarely severe for more than twenty-four hours.

A more severe serum reaction is sometimes seen, although instances are rare. Such a severe reaction may occur in a particularly susceptible individual after the first injection, but is seen more often after a second injection made during the period from about twelve days to three months after the first. In such cases the reaction appears immediately, from within a few minutes to within a few hours after the injection. There is marked malaise and muscular pain. Severe edema and erythema rapidly appear at the site of the injection, more rarely a marked edema of the face, a general urticaria, and occasionally marked dyspnea and threatening collapse, are seen. Usually these manifestations subside rapidly. In a very few instances sudden death has followed the injection of antitoxin, but the evidence has not always been clear that the injection was the cause of death. In a few cases, however, the death seemed to be due to the serum injection. In so many of these cases the patients have been asthmatic, that the association cannot be accidental, and some of them have been known to have the form of asthma which is undoubtedly an anaphylactic phenomenon, excited by contact with horses.

I have not space in this book to go into a full description of the phenomenon of anaphylaxis on which the untoward manifestations of serum therapy depend. The reaction depends upon the fact that the horse serum acts as a foreign body, against which the human organism forms antibodies, which are produced in from seven to twelve days after the injection, and which cause the toxic manifestations through a rapid splitting of the foreign protein. In cases in which a rapid severe reaction is seen, the tissues are so sensitive that they form antibodies with great rapidity. Such sensitiveness may be a constitutional peculiarity, or may have been produced by a previous injection.

The question has been raised whether the possible dangers from anaphylaxis are sufficiently great to affect the indications for serum therapy. Certainly in a dangerous disease like diphtheria, the possibility of serum sickness should not deter the physician from using antitoxin as early as possible in every case. The only exception would be in a known asthmatic, to whom it is better not to give horse serum in mild cases of diphtheria. The possibility of anaphylaxis has led some authorities to advise against the use of *immunizing* doses of antitoxin, on the ground that in susceptible individuals serious symptoms have followed small doses, and that the risk should not be taken until clinical diphtheria is actually present. Furthermore, anaphylactic phenomena are seen most often after a repetition of

the serum injection, and an immunizing dose would be a source of danger if a subsequent therapeutic dose ever became necessary. In my opinion the danger from anaphylaxis is too slight to counter-balance the advantage to be derived from immunizing injections of antitoxin. The routine practice at both the Children's and Infant's Hospitals for years was to give an immunizing dose to every patient admitted, and to repeat the injection every three weeks as long as the child remained in the hospital. Instances of severe anaphylactic manifestations have been exceedingly rare. Immunizing injections, however, should never be given to asthmatics. Furthermore, in children the use of the Schick reaction has greatly reduced the number of cases in which immunizing antitoxin injections are indicated.

GENERAL MEASURES IN DIPHTHERIA.—The general measures of nursing and hygiene which are used in any severe acute illness, are applicable to diphtheria. Fresh air and sunlight are particularly important. Diphtheria patients should be kept in bed throughout the entire attack, and for a longer period during convalescence than is required after any other acute illness of the same comparatively short duration. As long as there are any signs of cardiac weakness, as long as the child has not regained its strength, absolute rest in bed should be continued, even though fever and local symptoms have been gone for weeks. The child must be got out of bed gradually, the heart being carefully watched.

The nutrition of diphtheria patients is often a matter of considerable difficulty. Anorexia is frequently extreme, both on account of the pain on swallowing, and on account of the septic condition of the child and the ease with which vomiting is produced. Milk is the main reliance; it should not be diluted unless distinct symptoms of indigestion are produced. Cereal gruels may be given to older children. Fresh fruit juices are often better taken than water, and plenty of fluid is required. In severe and protracted cases, beef juice should be added to the diet. As convalescence comes on, zwieback scraped beef, bread, eggs, and so forth, are gradually added, till the child returns to its normal diet. Breast-fed infants with diphtheria should not be put to the breast, but should be fed with breast-milk obtained with the breast-pump.

When anorexia is very severe, it is sometimes better to give nourishment in small amounts more frequently; but it is better not to disturb the child oftener than every two hours. In obstinate cases, it is necessary to resort to gavage.

In children who have been intubed, or who have post-diphtheritic paralysis, the swallowing of fluids is often more difficult than that of foods of more solid consistency. In such cases junket, milk toast and jellies are useful.

Stimulation.—Owing to the action of the diphtheria toxin upon

the circulatory system, stimulants are frequently required. The indications for stimulation are a very rapid, feeble, or intermittent pulse, a weak first heart sound, and marked prostration. The stimulants which have formerly been most widely recommended in diphtheria are alcohol and strychnine. As a result both of clinical experience with these drugs, and of recent experimental work upon their action as circulatory stimulants, I have given up their use in the acute stage of diphtheria. Much better are the drugs whose value as circulatory stimulants has been adequately proven, namely, *caffein*, *camphor* and *digitalis*. In the acute stage, the best routine stimulant is caffein-sodium benzoate or salicylate, given in doses suited to the age of the patient. (See Division II.) Digitalis is useful when cardiac weakness persists after the acute stage. Camphor in oil is indicated in sudden threat of cardiac failure. In severe collapse with cold extremities and cyanosis, due to vaso-motor paralysis, adrenalin is useful. Alcohol is most useful in cases where nutrition is difficult and prostration prolonged. Strychnin in small regular doses three times a day should be used in the treatment of post-diphtheritic paralysis.

There are few other symptoms beside circulatory weakness in diphtheria which require internal medication. The giving of drugs is disturbing to the child, no drug influences the course of the disease, and all drugs should be avoided except necessary stimulants.

LOCAL TREATMENT.—Since the introduction of serum therapy, the local treatment of diphtheria has retired into the background. The painting and spraying of the throat, which was formerly recommended, is bad practice, and can do harm. Local treatment should not be entirely abandoned, but its benefits are not great enough to warrant its use when it encounters marked resistance on the part of the child, as the exhaustion caused by resistance is more harmful than any condition which local treatment can remedy.

The mouth can usually be kept clean by alkaline washes, without causing resistance. Older children can often gargle the throat with a solution of boric acid, or Dobell's, or Seiler's solution, or with a one per cent solution of hydrogen peroxide. In younger children the same solutions can be used for syringing the mouth and throat, unless this causes great resistance. I do not believe in syringing through the nose in diphtheria. Even in septic cases with a profuse fetid discharge, nasal syringing should only be used in exceptional cases. In nasal diphtheria one should rely mainly on serum therapy, and should rest content with removing as much secretion as possible with a cotton stick, and with protecting the upper lip with lanolin or some other simple salve.

For the painful swelling of the cervical lymphnodes, poultices

should never be employed. The application of cold by means of the ice bag is indicated in such cases.

CONVALESCENCE.—This is slow after a severe attack of diphtheria. No matter how rapid the apparent recovery, no patient should be allowed out of bed for at least a week after the disappearance of the membrane. The heart should be carefully watched. If the pulse remains abnormally rapid, slow, or weak, or is dicrotic or intermittent, if there is any weakness of the first heart sound, absolute recumbency in bed must be continued. A slight irregularity in the cardiac rhythm is not a contraindication to the child gradually getting about, provided that no other signs of cardiac weakness are present. The appearance of the typical post-diphtheritic paralysis also does not require the child to be kept in bed. As long as the child does not regain its full general strength, it should still be kept in bed.

Iron, and other tonics are sometimes indicated in convalescence for anemia or malnutrition.

The persistence of diphtheria bacilli in the throat is occasionally an annoying feature of the convalescence. Sometimes positive cultures continue to be obtained after the child has become fully convalescent, and this prevents release from quarantine. The best means of getting rid of the bacilli is to syringe through the nose three or four times daily, and in addition, children old enough should gargle frequently. Simple salt solution, Dobell's solution, or boric acid solution should be used. It is doubtful if the dilute solutions of bichloride of mercury (1 to 10,000) sometimes recommended, have any real antiseptic value.

TREATMENT OF LARYNGEAL DIPHTHERIA.—In the early stages of laryngeal diphtheria, before obstruction has become marked, the physician, while waiting for serum therapy to produce its effect, may try local measures before resorting to operative treatment. A warm pack is sometimes useful. Hot fomentations should be applied to the region of the larynx. The use of steam by means of the croup kettle and bed tent, as employed in common croup, may be tried. An emetic dose of ipecac may be given, as for common croup. The opiates, however, should be avoided.

If in spite of these measures, the obstruction shows a tendency to increase, the physician must be prepared to resort to operative interference. No hard and fast rule can be laid down as to when operation is indicated. More harm has been done by waiting too long than by operating too early. One should never wait for the appearance of cyanosis, as this sign is a precursor of death. In general when the obstruction is increasing, and has resulted in marked supraclavicular and epigastric inspiratory retraction, or if the ob-

structed breathing appears to be exhausting to the patient, or if there is any tendency toward somnolence or toward suffocative attacks, interference should not be longer deferred. Some German writers state that the moment for interference can be definitely fixed at the time when the sterno-cleido-mastoid muscles are brought into action as auxiliary muscles of respiration, the contraction with inspiration being detected by palpation.

When operative interference becomes indicated, the question which formerly had to be decided was whether to use *intubation* or *tracheotomy*. It is now generally recognized that intubation is the best primary operation for the relief of membranous laryngitis, tracheotomy being reserved for those cases in which for some reason intubation fails. The drawbacks to intubation are annoyances rather than real evils; the most conspicuous occasional troubles being obstinate difficulty in swallowing, repeated coughing up of the tube and ulcerations from pressure. The drawbacks to tracheotomy are the necessity of narcosis and trained assistance, the danger from hemorrhage and wound infection, the long period before the canula can be removed, and the frequency of sequelae such as disturbance of voice, decubitus, and tracheal stenosis.

INTUBATION

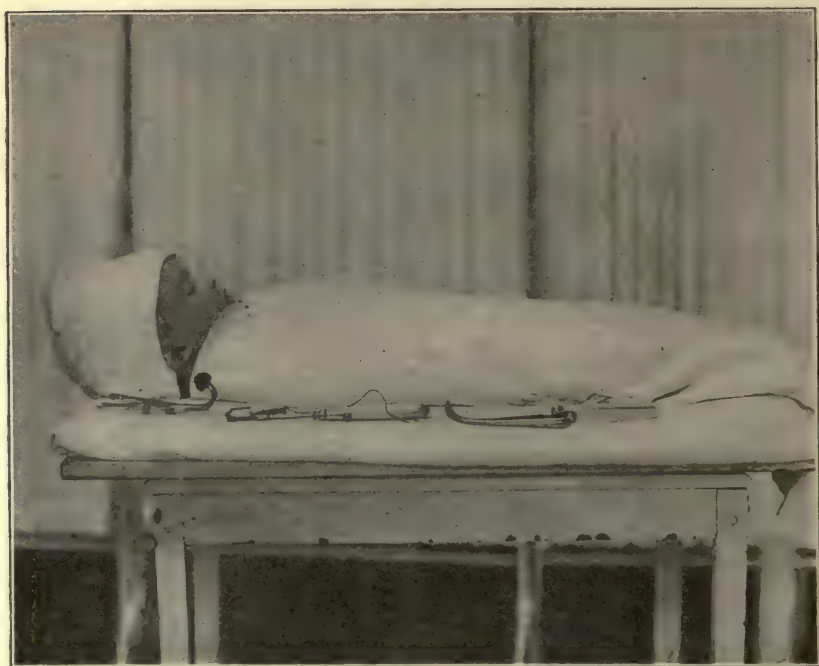
Intubation is the introduction through the mouth into the larynx of a tube of special construction. The instruments and technique were devised by Dr. Joseph O'Dwyer of New York, and were so perfected by him, that practically no improvements have since been added.

An intubation set consists of seven tubes of graded sizes, an introducer, an extractor, a mouth-gag and a gauge. The tube is selected according to the age of the patient, as indicated on the gauge. A large child often requires a larger tube than the one called for by its age.

TECHNIQUE OF INTUBATION.—The patient is wrapped firmly in a blanket, so that he cannot move his arms, and then placed in a horizontal position, with the head slightly raised. The mouth is held open by the gag, with its jaws resting on the molar teeth. The gag should be on the left side. Care must be taken not to have the cheek injured by the gag, and special pains must be taken to prevent its slipping. The head should be steadied by the assistant who holds the gag. The operator takes the introducer carrying the tube in the right hand with the index-finger around the hook on the under surface of the handle, the loop of silk passing over his little finger, and his thumb resting on the button on the upper surface of the handle. The index-finger of the left hand is then passed down to the epiglottis, which is hooked forward. The finger on entering the

pharynx is brought forward until it encounters the upper border of the cricoid cartilage which is felt as a hard nodule, and is a useful landmark. The epiglottis lies immediately in front, and should be drawn strongly forward. The tube is now introduced into the mouth, the handle of the introducer being well down on the chest of the patient. The tube is kept vertical in the middle line, and its tip is passed down the radial side of the left index-finger which serves as a guide, the handle of the introducer being raised to permit the tube to follow the course of the finger. When the tip of the tube approaches the tip of the finger, the operator moves the finger slightly toward his left while still maintaining the forward pressure on the epiglottis

FIG. 135



Apparatus for intubation

and tongue, and raises the handle of the introducer to a vertical position, which allows the tip of the tube, still following the radial side of the finger, to enter the opening of the larynx. It is best to choose for this moment of introduction, an inspiratory effort on the part of the child, as at such a time the glottis opens most widely. When the tube has entered for about one-third of its length, the operator should feel around it rapidly with the left index-finger, in order to be sure that it is in the proper position. If it has entered properly, it will be closely surrounded by a ring of soft tissue. The

right thumb then presses forward the thumb-piece, disengaging the introducer, which is withdrawn. The left index-finger is placed on the head of the tube, and pushes it down into place. It is well before withdrawing the finger to make sure once more that the tube is tightly surrounded by a ring of soft tissue. Further signs that the tube is properly in place are a peculiar hissing breathing sound, a paroxysm of coughing, and relief of the dyspnea. While waiting for these signs the operator passes the silk loop about the ear of the patient, and removes the gag.

The silk loop is best left attached to the tube, whenever there is evidence of loose membrane below, or when the patient is to be left in the care of someone who would not be able to remove the tube with

FIG. 136



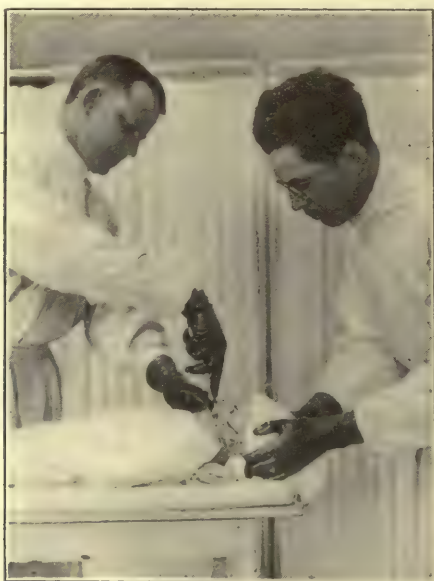
Intubation. Beginning the insertion of the tube

the extractor in case it should become obstructed. In such a case the silk passes out at the corner of the mouth, and is attached to the cheek with a piece of adhesive plaster. The child's hands must then be secured so that he cannot seize it. When anyone is to be constantly within reach who is competent to use the extractor, it is best to remove the silk loop from the tube. For this purpose one strand of the loop is cut, the gag is inserted a second time, the left index-finger is placed on the head of the tube, and the loop pulled through and free from the tube.

It cannot be overemphasized, that very little force is required for the passage of the tube into the larynx, no more than is used in the passage of a catheter through the urethra into the bladder. The operation must be performed quickly, as sometimes the holding of the mouth open with the gag will cause a cessation of respiration. The entire manipulation can be completed in a very few seconds.

The most common mistake made in intubation is the passage of the tube into the esophagus instead of into the larynx. This is recognized by the following facts: The finger in the pharynx does not find the posterior wall of the larynx between it and the tube; the tube can be pushed down indefinitely, instead of coming to a point where it can be pushed no farther down without depression of the

FIG. 137



Intubation. Completing the insertion of the tube

whole larynx, and it may continue to pass downward as shown by shortening of the silk loop; the hissing breathing, paroxysm of coughing, and relief of dyspnea do not occur. When these signs show that the tube has been passed into the esophagus, it is withdrawn by means of the silk loop, and after a few minutes a second more careful attempt is made.

False passages are sometimes made, the tip of the tube going into one of the ventricles of the larynx. It can be pushed quite through into the cellular tissue, but this would only happen from the use of the most brutal force. The cause of the tube entering the ventricle

is that the operator works from the angle of the mouth, instead of keeping the tube in the median line. A false passage of this kind is recognized by the fact that although the tip of the tube is felt to enter the opening of the larynx, it cannot be pushed down into place without undue force, and the head of the tube projects above the epiglottis. The tube must be withdrawn, and another attempt made, with care to keep tube and introducer always in the median line.

Rarely the operation of intubation shows all the signs of having been properly performed, except relief of dyspnea, and instead of relief, breathing appears to have become more or completely obstructed. This is serious, and usually means that loosened membrane has been pushed down ahead of the tube and is obstructing the larynx, though it may be due to an unskillful prolongation of the operation. The tube must be immediately withdrawn, and sometimes this is followed by a paroxysm of coughing in which the obstructing membrane is expelled. If this does not occur, give the patient half a teaspoonful of whiskey or brandy undiluted to excite cough. If there is still threatening asphyxia, try artificial respiration, and if no air enters, tracheotomy must be performed at once.

CARE OF INTUBED CASES.—The feeding of patients who have been intubed is sometimes difficult. Infants who take their food by sucking usually have no difficulty, but older children sometimes experience considerable difficulty in swallowing, especially in the taking of fluids. At other times the taking of fluids causes excessive coughing. In such cases the patient may be able to take semi-solid articles of food, such as cereal jellies, junket, ice cream, scrambled eggs and milk toast. The method of feeding suggested by Casselberry of giving fluids with the head lowered, has been widely recommended, but I have seen at autopsy an undoubted case of inhalation pneumonia after this method of feeding, and prefer other methods. Gavage is a preferable method, especially in the younger patients. Nutritive enemata may be an important adjunct in certain cases.

The tube is often coughed up prematurely. This may be due to the fact that the nurse has laid the child face downward, or held him over one shoulder; in both these positions the tube is very easily expelled. In some cases, frequent coughing up of the tube is due to the fact that too small a size has been used. When the tube is expelled, dyspnea may return at once, or may not return for several hours. When it appears, the tube must be replaced, a size larger being used if necessary. Occasionally the tube is coughed out of the larynx and swallowed. This need cause no alarm, as the tube is soon passed from the intestine without harm. When the tube is not coughed up until after two or three days, dyspnea often does not return, and the tube can be dispensed with.

The sudden blocking of the tube with membrane loosened from the trachea or bronchi may occur at any time after the introduction of the tube. This is ordinarily not serious, as the usual result is the immediate expulsion of the tube by coughing, followed by the discharge of the loose membrane. No definite rule can be given regarding the length of time that the patient should wear the tube. It is well to remove it at the end of the third or fourth day, but it is frequently necessary to reinsert it. In some instances three or four extractions and introductions may be required. The most favorable cases are those in which the child coughs up the tube at the end of the third day, and does not require reintubation.

FIG. 138



Intubation. Withdrawing the tube

REMOVAL OF THE TUBE.—The first steps of an extraction are similar to those of an introduction. The extractor is passed into the lumen of the tube and the lever on the handle pressed so as to open the jaws of the instrument, and the tube extracted by a reverse of the movements used in introduction. Sometimes there is considerable difficulty in extraction, but by patience and gentleness the end can be accomplished.

After a tentative removal of the tube the child must be carefully

watched, and if dyspnea recurs, the tube must be replaced. If after two or three hours dyspnea does not return, the tube can usually be dispensed with.

COMPLICATIONS OF INTUBATION.—There is always a certain amount of hoarseness, and sometimes aphonia, following intubation. This usually passes off within a week, sometimes persists for three or four weeks, but is never permanent.

There is also usually some superficial ulceration from pressure at the base of the epiglottis, and at the end of the tube in the trachea. This is not serious. Deep ulceration only occurs in poorly nourished children, usually in association with other serious complications of the disease.

In a very few cases after intubation, difficulty is encountered in dispensing with the tube. All attempts to remove the tube permanently are followed by recurrence of dyspnea. This does not occur nearly so often with intubation as after tracheotomy. In most cases, the patient can do without the tube in a few weeks, but occasionally a case is more obstinate. The cause is probably swelling and edema of the tissues, which have become the seat of chronic inflammation, and which swell when the pressure is removed. In a few cases cicatricial contraction from ulceration has been found. The condition is best treated by increasing the pressure by the insertion of larger and larger intubation tubes. Some cases may be so obstinate as to require tracheotomy.

The only serious accident which occurs with intubation is the sudden blocking of the tube with loosened membrane. When this cannot be relieved by removal of the tube and reinsertion, tracheotomy must be performed.

INDICATIONS FOR TRACHEOTOMY.—Tracheotomy is indicated only when for some reason intubation does not cause the necessary relief of symptoms.

PROBLEMS AND RESEARCH.—There are fewer unsolved problems of importance connected with diphtheria than with the majority of the other infectious diseases. Most of the important facts as to the organism, its transmission, its mode of entrance, its action in the body, and the mechanism of recovery and immunity are known. Much of the research in the past few years has been devoted to confirming the value of the Schick reaction as a measure of immunity and a means of studying natural immunity and the duration of the immunity produced naturally by infection, and artificially by anti-toxin injection. The result of this work has been incorporated in the description of the disease.

The following additional points have been the subject of study in diphtheria in the last few years:

1. Active immunization. 2. The dosage and mode of administration of antitoxin. 3. The relation of the toxins to diphtheritic paralysis. 4. The mechanism of circulatory failure. 5. The treatment of diphtheria carriers.

ACTIVE IMMUNIZATION.—It has been known for many years that a vaccine composed of a mixture of toxin and antitoxin could be used to produce an active immunity in animals. Von Behring began experimenting with the use of toxin-antitoxin mixtures in immunizing children in 1912, publishing his report in 1913. Since then a number of studies have been made, the observations of the different observers not being uniform. The results of many of the investigations have been judged only by the percentage of exposed cases which acquired the disease, and this is a very unreliable method of estimating the results. Park, Zingher and Serota have reported their experiences in producing active immunity by this method, controlling their results by determining the antitoxin content of the blood before and after injections of vaccine. The antitoxin content was estimated both by Römer's intracutaneous method and by means of the Schick reaction. They found that in susceptible persons, active immunity may be produced after a period of from two to six weeks. Persons already immune through having a supply of natural antitoxin in the blood, showed a decided increase in the antitoxin content as a result of the injection in a relatively short time, but of course such patients do not require active immunization. Of the remainder, those not showing natural immunity, less than 25 per cent reacted to the diphtheria toxin and antitoxin mixtures to a sufficient degree to be thoroughly immunized. Of the 75 per cent which could not be perfectly immunized, only 20 per cent of the exposed contracted the disease. It would seem therefore from the results of these studies, that the use of toxin-antitoxin injections is not certain enough to supersede passive immunization. The matter stands at present about as it did before, namely, that the Schick reaction should be used to determine immunity, and that every exposed patient having a positive reaction should receive an immunizing dose of serum.

THE DOSAGE OF ANTITOXIN.—Most of the work on this subject has been devoted to demonstrating the superior value of massive doses. Most of the evidence used in support of this contention is in the form of mortality statistics, which are of course very unreliable as proof. It is generally agreed that the object of treatment is to give a sufficient amount of antitoxin to neutralize the toxin in the body. Schick, Kassowitz and Busacchi, as a result of their experiments, believe that it is possible to calculate the amount of antitoxin needed according to the body weight of the individual to whom it is to be given. All of this work emphasizes the importance of early

injections. It has been clearly shown that the absorption of anti-toxin, whether the serum be injected subcutaneously or intramuscularly, is slow. The most valuable suggestion of the last few years has been the use of the intravenous route in injecting diphtheria anti-toxin, and the superior value of this method of injection has been demonstrated experimentally.

THE RELATION OF TOXINS TO DIPHTHERITIC PARALYSIS.—The theory of Erlich that the paralysis is caused by the toxone, while the general poisoning is caused by the toxin, has been supported by recent work. It has been shown that there is no relation between the size of the dose of toxin necessary to produce death and that which produces paralysis. Apparently the power of diphtheria toxin to produce paralysis and to produce death, are distinct features. It has also been demonstrated again that antitoxin never causes paralysis *per se*. The apparent increase of the number of cases of post-diphtheritic paralysis since the introduction of antitoxin is due to the decreased mortality of diphtheria, which allows many severe cases which would formerly have died and which are most likely to have paralysis, to live. Recent work has also shown that the use of antitoxin when given early enough, tends to prevent paralysis. The superior value of the intravenous route was also clearly shown in these experiments.

MECHANISM OF THE CIRCULATORY FAILURE IN DIPHTHERIA.—In all the fatal acute infections, this subject is receiving considerable study at the present day. It is known that in most of the acute infections the phenomena which precede death closely resemble those seen in surgical shock, and they have been attributed to vasomotor paralysis. In diphtheria, however, the symptoms have been almost exclusively attributed to the action of the toxin, either on the heart muscle itself, or on the nervous mechanism governing the action of the heart. Hardly more than a beginning has been made in these studies, but much will probably appear in the course of the next few years. Some recent work of MacCallum tends to show that the death which occurs in the height of an attack of diphtheria is not exclusively the result of direct injury to the heart.

THE TREATMENT OF CARRIERS.—The best means of getting rid of the bacilli in the throats of diphtheria carriers is an important matter, and has been the subject of many suggestions. Up to the present time, no very effectual method which is not objectionable in some way or another, has been found. It is probable that this question will be the subject of much further study. Among recent suggestions there is one of Miller, which recommends spraying the throat with a solution varying in strength from $\frac{1}{4}$ to 1 per cent of the usual 40 per cent formaldehyde solution. Another method which has been reported to have given good results is the spraying of the throat

with a suspension of the staphylococcus aureus in salt solution. We shall have to wait longer, however, before any one of these measures emerges as preëminent.

PERTUSSIS

(Whooping-Cough)

Pertussis (whooping-cough) is a specific infectious disease, highly contagious, affecting the respiratory tract, characterized by periods of spasmodic coughing succeeded by a prolonged inspiration and accompanied by a peculiar sound called the "whoop."

ETIOLOGY. THE MICROÖRGANISM.—The specific cause of whooping-cough is a bacillus, first described by Bordet and Gengou in 1900, and obtained in pure culture in 1906. Until the work of Mallory, the proof that the Bordet-Gengou bacillus is the specific cause of whooping-cough depended upon the following facts: 1, the organism is found in large numbers, sometimes even in pure culture, in the sputum of all early cases; 2, similar appearances in the sputum are not found in other conditions; 3, the serum of whooping-cough convalescents agglutinates the organism; 4, the serum of whooping-cough patients gives a complement fixation test specific for the organism.

While the Bordet-Gengou bacillus was accepted as the cause of whooping-cough by the majority of authorities, its etiological relation could not be regarded as fully proved. The obstacle to the complete fulfillment of Koch's laws was the absence of any anatomical lesion characteristic of whooping-cough. Furthermore, the clinical picture produced in monkeys by inoculation with cultures of the Bordet-Gengou bacillus, while sometimes suggestive, was not sufficiently typical to be regarded as certain confirmation.

In 1912, Mallory and Horner announced the finding of a definite anatomical lesion characteristic of whooping-cough, the essential lesion being the presence of masses of a minute bacillus between the cilia of the bronchi. These organisms morphologically and culturally resembled the bacillus described by Bordet and Gengou. Mallory was able by intratracheal inoculation to reproduce the same lesions in animals. In puppies, the lesions were also reproduced by contagion. This work supplied the missing links in the chain of proof needed to establish the causal relation of the bacillus to whooping-cough, giving the complete fulfillment of Koch's laws. The only possible remaining doubt is whether the Bordet-Gengou bacillus represents a single organism, or a number of organisms of similar morphology and cultural characteristics. In view of the specific contagiousness of whooping-cough, it is probable that any differences in the finer biological reactions of the bacilli are no more than have often been found in different strains of the same organism.

The bacillus which causes pertussis is a minute ovoid non-motile cocco-bacillus, closely resembling in size and in appearance the bacillus of influenza, but not requiring the presence of hemoglobin for its growth in cultures. It is Gram-negative, and stains only slightly by ordinary methods, especially in the center of the organism. The organism can be grown at the start only on the potato blood-agar medium devised by Bordet, though after continued cultivation it will grow to some extent on other media. The growth is slow, forming minute transparent colonies. In cultures the organism is round or oval, and resembles a coccus more than a bacillus. It is not resistant toward high temperatures.

The organism is found only in the respiratory tract; its absence in the blood has been demonstrated. That it forms some toxin is shown by the slight inflammatory reaction which it produces, and by the formation of an antibody which gives the complement fixation test. Toxin formation is comparatively slight, and probably plays little or no part in producing the characteristic symptoms of the disease. Mallory has suggested that the action of the bacillus is chiefly mechanical, and this at present seems the most plausible hypothesis. Some writers believe in a neurotic factor in etiology, but this probably plays no more than a possible rôle in influencing the severity of the clinical manifestations.

TRANSMISSION.—The spreading of whooping-cough occurs almost exclusively directly from one case to another. The contagium is air-borne, the bacilli being contained in the moist particles expelled in coughing—the method of “droplet infection,”—and entering with the inspired air. The sputum contains enormous numbers of bacilli, so that a very brief stay in the presence of a whooping-cough patient is sufficient for transmission. The disease is consequently very highly contagious. Indirect transmission, the carrying over of the bacilli by means of healthy carriers, clothing, and contaminated objects, occurs very rarely if at all.

THE INFECTIOUS PERIOD.—Whooping-cough is contagious from the very beginning of the so-called catarrhal stage, and the disease can be and usually is transmitted during the period of one or more weeks before the nature of the disease has been made clear by the appearance of typical paroxysms. The transmissibility of the disease is greatest at this early period, but the disease remains contagious through the earlier part of the convulsive stage. Its communicability diminishes rapidly during the latter part of this stage, and is slight or absent after the paroxysms cease. It is well, however, to regard whooping-cough as still possibly contagious as long as cough is still present.

PREDISPOSITION.—The susceptibility toward whooping-cough is

very great, being comparable with that toward measles and vari-cella. There is no evidence of any natural or constitutional immunity at any age. Given sufficient exposure, children who have not had the disease are practically certain to acquire it.

This susceptibility is seen at every period of life. Whooping-cough occurs most often in the first three years of life. It is somewhat less common in the first year than in the next two years, but in no other specific infection is infancy so susceptible as in whooping-cough. The disease is often seen in the earliest months of infancy, sometimes in the earliest weeks. It has been described in newborn infants whose mothers had the disease. It is probable that there is no inherited immunity which protects children in the first year, such as is seen in other contagious diseases. The lesser frequency of whooping-cough in the first year is to be explained, not by a lesser susceptibility, but by the fact that young infants are better isolated and protected from exposure, and that many, being first babies, do not encounter exposure at all.

Whooping-cough continues to be comparatively common through childhood, the frequency growing less with increasing age. It is rare in adults. These phenomena are, however, not due to a progressive decrease in susceptibility, but to the fact that in so highly contagious a disease immunity is acquired early in life.

Constitutional peculiarities have no real influence on the susceptibility toward whooping-cough, except that girls appear to be more susceptible than boys. It is often stated that children liable to catarrhal affections of the respiratory tract are more susceptible. This cannot be proven, because all children are so susceptible anyway. Neurotic and spasmophilic children are not more susceptible to infection, but in them the paroxysms are apt to be more severe and the disease to last longer. Debilitated children with low resistance show the influence of constitutional peculiarity in the liability toward complications.

EPIDEMIOLOGY.—As in most of the more highly contagious diseases, the frequency and severity of recognizable epidemics depends on the population of the place. Epidemics are only seen in small or isolated communities. In the large centers of population whooping-cough is present at all times and so large a proportion of the population are immunized that epidemics do not occur.

The disease is somewhat commoner in the winter and spring than in warm weather. This may be due to the greater prevalence of respiratory affections.

IMMUNITY.—An attack of whooping-cough confers a high degree of immunity, so that second attacks are rare. They are seen at times, however, and are rather more frequent than in the exanth-

mata. Second attacks are almost never seen in childhood, but are commonest in adults who had whooping-cough in childhood, and who are brought into close and long continued contact with children sick with the disease. The greater susceptibility of the female sex is particularly noticeable in connection with these occasional second attacks in adults.

INCUBATION.—The incubation period of whooping-cough is difficult to determine, because the onset of the disease can be less definitely timed than in other contagious affections. It appears to be of varying length. The average length is one week, but the period may be only half this time, or may extend to two weeks. When exposure is suspected, it is safe to assume that if after fourteen days there are no catarrhal symptoms of any kind, infection has not taken place.

PATHOLOGICAL ANATOMY.—The essential lesion of whooping-cough, and the only one peculiar to the disease, is the presence of masses or clumps of bacilli between the cilia of the trachea and bronchi. There is some infiltration of the submucosa with lymphocytes and plasma cells (Mallory), and some invasion of the epithelium with polymorphonuclear leucocytes.

Changes in the blood are constant in whooping-cough, but are not peculiar to the disease. There is a leucocytosis, the lymphocytes showing a marked absolute and relative increase.

The other lesions found at autopsies are either due to some of the mechanical effects of the disease, or to complications. Death is always due to some complication. Among the mechanical lesions are extreme congestion of various organs, such as the meninges, lungs, heart and kidneys; hemorrhages in various regions, such as the eye, or the meninges; emphysema, either of the lung, or of the mediastinal or subcutaneous tissue from rupture of the alveoli. The commonest complications are bronchopneumonia, with its associated lesions, and the lesions of the secondary stage of tuberculosis.

SYMPTOMS.—It is customary to divide the disease into three periods,—the *catarrhal stage*, the *spasmodic stage*, and the *stage of decline*. It must be remembered, however, that such a division is somewhat arbitrary and inexact, as the three periods overlap and run into one another. It is only made for convenience of description.

The symptom complex of pertussis is very constant, varying mainly in the severity of the case. The description as here given applies to a case of medium severity.

THE CATARRHAL STAGE.—The symptoms in the beginning and often for several weeks, are simply those of a bronchial catarrh, or common cold, with cough, and perhaps some sneezing, hoarseness, or reddening of the conjunctiva. These symptoms usually last from one to two weeks, though at times typical paroxysms may appear in

less than a week, or not for four weeks. In the very beginning in some cases there may be a slight rise of temperature. During this stage the disease cannot be differentiated from an ordinary cold, and whooping-cough can only be suspected when there has been a known exposure. A few cases, which subsequently are recognized as whooping-cough by transmitting the disease, never show spasmodic symptoms, but pass through the disease unrecognized. In most cases, however, the cough becomes more violent. The disease may often be suspected at this time because the cough begins to occur at more or less regular intervals by night as well as by day, and resists the ordinary means of treatment, and also because in spite of the severity of the cough, no râles are heard on auscultation of the lungs.

THE SPASMODIC STAGE.—The transition from the catarrhal to the spasmodic stage is gradual. The cough becomes *less frequent*, but *more violent*. The attacks of coughing become paroxysms, which occur at more or less regular intervals, the child being entirely free from cough in between. These attacks, sometimes quickly, sometimes more gradually, develop into the typical whooping-cough paroxysms.

The child often experiences premonitory symptoms, either a tickling in the throat, an oppression in the chest, or a general feeling of anxiety. These cause restlessness, the child runs to its mother, or holds itself fixed on its chair. Then, after a deep inspiration, occurs a succession of forcible expiratory coughs, occurring in rapid staccato, *without any inspiration occurring between them*. During the paroxysm the face becomes red, the conjunctivae become congested, and the tongue protrudes from the mouth. Finally there occurs a long-drawn crowing inspiration, in which the air is drawn through the spasmodically contracted glottis, causing the peculiar *whoop*. The attack is, however, usually not ended with this occurrence, but is immediately repeated, and this may occur a number of times. With each repetition the lips and tongue become more and more cyanotic. In severe cases, the eyes protrude, cyanosis becomes very marked, and the child looks as though it would die of asphyxia. The attack usually ends with the expulsion of a little tenacious mucus, which in older children trickles out of the mouth, and in young children often stays in the larynx. With the expulsion of this mucus, vomiting frequently occurs, especially after the severer paroxysms. Strong older children recover rapidly from the attack, and often immediately resume their interrupted play. Weak children and young infants are left exhausted and bathed in sweat, and require more time for recovery.

The number and severity of the attacks show the widest variation in different cases. Some children have only four or five in twenty-four hours, while others may have thirty, forty, or fifty. The severity

of the single attack also varies widely; sometimes the paroxysms of cough and whoop are only repeated two or three times, while at other times they may be repeated ten times or more. It is to be remembered that these variations are seen not only in different children, but also in an individual case, a fact which must be remembered in estimating the value of any method of treatment.

The duration of the spasmodic stage is also very variable. It is usually three or four weeks, or even more, but may be shorter.

The lungs in uncomplicated cases are normal to auscultation and percussion. There may occasionally be a few coarse bronchial râles, which disappear temporarily after a paroxysm. In infants, signs of pulmonary emphysema may develop during the spasmodic stage.

FIG. 139



Pertussis during paroxysm. Female, 4 years old

THE STAGE OF DECLINE.—The paroxysms become first less frequent, then less severe. Vomiting ceases. Finally the cough only rarely occurs, and has lost its typical character. A simple catarrhal cough may, however, persist for a number of weeks longer.

The duration of the entire disease is variable; in average cases it is from six to ten weeks, but may be three or four months, even in uncomplicated cases. A certain amount of loss of weight is the rule, but this is rapidly recovered in convalescence, if there is no complication involving the lungs. If during the stage of decline

bronchitis occurs, or even if the child simply catches a simple cold, there is an apparent relapse into the spasmodic stage, the paroxysmal cough returning with all its typical features, and persisting until the bronchitis or cold is recovered from. The same thing may happen after complete recovery, and if a child in the course of the succeeding months, even as long as a year, has any cold or other affection characterized by cough, the cough assumes a paroxysmal character, and even the whoop may reappear.

ATYPICAL CASES.—Very mild cases are seen at times, in which the attacks are rare and not easily recognized as whooping-cough, and in which the duration of the disease is only two or three weeks. In many cases, no whoop is heard at any time, and the paroxysms may be so mild and atypical as not to be suggestive. These mild cases can often be diagnosed only by the presence of whooping-cough in the neighborhood.

Very severe cases of uncomplicated whooping-cough are rare. Occasionally, however, a case is seen which from the onset shows high fever, and marked affection of the general condition through restlessness and loss of sleep. Vomiting becomes very frequent, dyspnea appears, the pulse becomes very rapid, and in younger children, death may occur.

Whooping-cough as seen in the younger infants is often peculiar in its manifestations. The paroxysms are severe, leading to cyanosis, and often producing a brief period of apnea, with disturbance of the consciousness and convulsive movements. At the same time the whoop is absent, the paroxysm ending with gagging and the trickling out of the mucus. Vomiting is less frequent.

SINGLE SYMPTOMS.—There are a certain number of symptoms which do not form part of the constant clinical picture of whooping-cough, but which are seen with more or less frequency. Many of them are the result of the mechanical effect of the severe paroxysms, which produces venous stasis.

In severe cases the heart shows enlargement of the cardiac dulness to the right, due to dilatation of the right ventricle. The pulse in such cases becomes more rapid, and there may be a blowing systolic murmur at the apex. These signs disappear in the stage of decline. After the disease has lasted for some weeks, there is often a certain amount of edema of the face, especially under the eyes. Fever is usually absent throughout uncomplicated cases, except sometimes early in the catarrhal stage. Occasionally there is slight fever throughout the disease.

Ulceration of the frenum of the tongue from pressure on the teeth during the paroxysm, is not uncommon, especially in infants who have only the two lower middle incisors. Involuntary passage of

urine and feces, and sometimes prolapse of the rectum, are occasionally seen during the paroxysms.

The nervous system has a marked influence on the course of whooping-cough. The paroxysms are precipitated by nervous excitement or by an irritation in the throat or the respiratory tract, such as may result either from swallowing or from the inhalation of dust. In nervous and neuropathic children the paroxysms are also more severe, and anything in the surroundings of the child tending to stir up the nervous system may have a marked influence in increasing the severity of the disease.

The digestive system is usually but little affected in whooping-cough, except for the vomiting at the end of the paroxysm. This may, however, be very obstinate, and may seriously interfere with nutrition. Diarrhea is very rare.

Albuminuria, due to congestion of the kidneys, is occasionally seen in severe cases.

THE BLOOD.—The changes in the blood of pertussis have been carefully studied in the last few years, and are important in diagnosis. The principal phenomenon is a leukocytosis, the white count being from 20,000 to 40,000, averaging about 27,000. There is an absolute increase in both the neutrophiles and the basophiles, but the increase in the basophiles is the most marked, so that there is a relative increase of the basophiles shown in the differential count. These changes begin in the catarrhal stage, and are most marked in the early part of the spasmodic stage.

COMPLICATIONS.—The most serious and important of the complications of whooping-cough are *hemorrhages*, *bronchopneumonia*, *tuberculosis*, and *disturbance of the nervous system*.

HEMORRHAGES.—Hemorrhages, as a result of the marked venous stasis produced by the paroxysm, are not very uncommon. Epistaxis is the most frequent form, but is seldom severe enough to be threatening. Occasionally blood is coughed up from the pharynx or bronchi. Hemorrhage into the conjunctiva, forming a crescent around the cornea, is relatively not uncommon. Hemorrhages into the eyelids, or into other parts of the skin, are more rare.

Occasionally the mechanical effect of the whooping-cough paroxysm may produce a hemorrhage into the central nervous system, usually involving the meninges, resulting in sudden hemiplegia, monoplegia, or some other disturbance, such as aphasia, facial paralysis, or some disturbance of the sight, hearing, or sensation. The hemorrhage may be fatal. Such cases are fortunately rare.

BRONCHOPNEUMONIA.—Bronchitis of the larger bronchi, as shown by coarse sonorous râles, is so frequent in the severer cases of whooping-cough, that it is usually considered a symptom rather than a

complication. As many children with whooping-cough have no râles at any time, I believe that any bronchitis strictly speaking is a complication, and the bronchitis of the larger bronchi is often a forerunner of a more severe form.

Bronchopneumonia is always preceded by a bronchitis of the smaller tubes, and it is usually difficult clinically to distinguish the two conditions. It is much more common in infants than in older children. The onset of a severe bronchitis in the course of whooping-cough, is marked by the appearance of moderate fever, of ordinary catarrhal cough between the whooping-cough paroxysms, and of a more abundant, greenish-yellow sputum. When bronchopneumonia develops, it is recognized by the appearance of a higher temperature, which is irregular and remittent, and by the appearance of rapid breathing. Often the whooping-cough paroxysms lose their typical characteristics, becoming shorter, with disappearance of the whoop, although the cyanosis may be still more marked.

The signs in the lungs are those of any secondary bronchopneumonia, diffuse crackling râles, with or without areas of dulness and bronchial breathing. The course is that of a secondary bronchopneumonia, but is apt to be severe and of long duration, owing to the weakened condition of the child. Bronchopneumonia is the most frequent cause of death in whooping-cough.

The bronchiectasis and emphysema of the lungs, which are such frequent findings at autopsy, are not often to be recognized clinically. Occasionally, however, there is a rupture of the alveoli which causes an interstitial emphysema of the mediastinum, in which the cardiac dulness is entirely replaced by tympany. Exceptionally there may be a subcutaneous emphysema which, beginning near the neck, may spread widely over the body. Emphysema may be recovered from, or may lead to severe dyspnea and death.

TUBERCULOSIS.—It is generally recognized that children who have recently had whooping-cough, are liable at times to develop some serious form of tuberculosis. This does not mean, as many wrongly suppose, that whooping-cough predisposes children to become infected with tuberculosis. The cases which apparently develop tuberculosis as a complication or sequela of whooping-cough have been infected with tuberculosis at a much earlier date, and when they contract whooping-cough, already have in their bodies the lesions of the primary stage of tuberculosis. The whooping-cough lessens their resistance to the spreading of the disease, and favors the development of the secondary tuberculous lesions. The commonest of these secondary manifestations seen in whooping-cough is tuberculous bronchopneumonia, but tuberculous meningitis, or general miliary tuberculosis, is seen at times.

DISTURBANCES OF THE NERVOUS SYSTEM.—The gravest complications of whooping-cough which involve the nervous system have already been enumerated among the hemorrhages.

In younger children the paroxysms often precipitate a laryngeal spasm similar to that seen in spasmophilia, and occasionally eclamptic attacks with loss of consciousness are also seen. Laryngeal spasm with a convulsion may conclude each paroxysm. Eclamptic attacks may even occur between the paroxysms. It is probable that these manifestations are seen mainly in spasmophilic children, the pertussis acting as a precipitating cause. Whooping-cough may prove fatal in cases of spasmophilia with laryngospasmus.

DIAGNOSIS.—The diagnosis of whooping-cough in the spasmodic stage is usually easy, provided that the physician can hear a paroxysm. If, however, the child has no paroxysm during the visit of the physician, a positive diagnosis is impossible. The physician must judge by the description of others, which is apt to be misleading. It is often possible to provoke an attack, either by introducing a spoon or spatula into the mouth as for examination of the throat, pressing strongly downward on the tongue, or by pressure on the larynx or trachea. If a paroxysm cannot be elicited, and if the intervals between attacks are long, the physician is compelled to base his diagnosis on the history. If the typical whoop be present, the description is often sufficiently characteristic for a diagnosis, but if, as often happens, especially in infants, there is no whoop, there may be considerable doubt. The following questions should be asked as having a special bearing on the diagnosis: 1, Does the cough come in long fits without the child drawing breath? 2, Do the attacks come at night as well as by day? 3, Is there any short cough in the intervals between the attacks, or in other words, is the cough always in long fits? 4, Is there vomiting, and if so does it come only with an attack of coughing? 5, Is there any expectoration? It should be remembered that in infants and young children up to the age of eight or ten years, expectoration is almost never seen except in whooping-cough. The diagnosis is supported at times by the absence of physical signs in the lungs in uncomplicated cases, by the absence of fever, by the story of severe congestion of the face in the attacks, by any visible hemorrhages, and by ulcer of the frenum of the tongue.

In the catarrhal stage, and in the spasmodic stage of mild and atypical cases, the diagnosis is much more difficult. Often a diagnosis can only be made when there is recognized whooping-cough in other members of the family, or a history of certain or possible exposure. The nearer the approach to the stage of typical paroxysms, the greater the possibility of suspecting whooping-cough. The examination of the blood often helps in the diagnosis of whooping-

cough in the catarrhal stage. In any cough in children, a high white count, without there being any fever, points toward whooping-cough. There are some secondary infections which give a high white count without fever, but the increase is usually in the neutrophiles, while in early whooping-cough the differential count usually shows a relative increase in the basophiles. Kolmer has reported a series in which whooping-cough in the catarrhal stage was correctly diagnosed by the blood examination in 81 per cent of the cases, and correctly excluded in 71 per cent.

The conditions which most often present themselves in the differential diagnosis of whooping-cough are certain ones involving the air-passages, such as adenoids, pharyngitis, laryngitis, bronchitis and tuberculosis of the bronchial lymph nodes. In the affections of the pharynx and larynx, while the cough may be severe and somewhat spasmodic, it is more frequent and irregular, and typical attacks do not develop. In bronchitis, the attacks of severe coughing come at the very beginning, instead of developing gradually, and are more frequent; also acute bronchitis is accompanied by fever and numerous râles in the lungs. In tuberculosis of the bronchial lymph nodes, the differential diagnosis is sometimes more difficult, as the cough is apt to be distinctly paroxysmal, and there may be expectoration or even vomiting. The whoop is, however, always lacking, and the cough lasts for many months without much change in its character or intensity. The other signs of tuberculosis, such as interscapular dullness, d'Espine's sign, positive von Pirquet reaction, and positive X-ray picture, are usually present in such cases.

PROGNOSIS.—Pertussis is a very serious affection in young infants, and also in older children who are debilitated or poorly cared for. This is because the liability to bronchopneumonia is greater the younger the patient, and both the frequency and fatality of this complication is increased by poor physique. When whooping-cough occurs in older children the prognosis is favorable, provided that they have previously been well and strong, that they are well cared for, and that no complications arise.

In many cases young infants, if their vitality is unusually good, and if they are carefully nursed and made to take a sufficient amount of food, show remarkable powers of resistance during attacks of pertussis.

PROPHYLAXIS.—While it is a fact that in spite of any precautions, almost all children will contract whooping-cough during some period of their childhood, it is not in my opinion ever justifiable to allow a child to become exposed to whooping-cough if it can be avoided. It is particularly important to protect children during the first four years of life, for it is at this age that the tendency to bron-

chopneumonia is greatest. Children, with whooping-cough should be strictly isolated, under the same conditions as are used in the prophylaxis of measles, which has the same mode of transmission. It is, however, undesirable that a whooping-cough patient should be confined to a single room, and it is therefore better, whenever possible, to send away the other children of the family, and to convert the house into a whooping-cough hospital, to which the other children can be brought back if they have become infected.

If one waits until the diagnosis of whooping-cough can be made before isolating the patient, the disease will have been already transmitted during the catarrhal stage to all the other children of the family. To approach efficient prophylaxis, it would be necessary to isolate a child every time it begins to cough, and to keep it isolated for several weeks, and this is manifestly impracticable, as colds and coughs are so common in early life, that such a procedure would compel school-children to spend much of their time in useless isolation.

The most practical method, one which I habitually employ with the patients under my care, is to isolate, not the school child with a cough, but the young child whom I wish to protect. When any one of the older children in the family has a cough, no matter how harmless it seems, the younger children, those under five years, are separated at once from the others, and are kept apart as strictly as the circumstances of the family will permit, until the cough has ceased. This will often enable one to protect young children, and to postpone the inevitable day when they must acquire whooping-cough to a period when the disease is fraught with less danger. It is on account of the danger of acquiring whooping-cough that I do not permit my patients to attend kindergartens until they are four or five years old. After this age, the advantages of kindergartens and companionship with children of the same age more than counterbalance the danger of contagious disease. As to how much very young children should be allowed to play with the children of friends, is a question to be determined by how careful the parents of the latter are in questions of hygiene and prophylaxis.

The other children of a family in which a case of whooping-cough has developed, should always be regarded as having been exposed, no matter how brief and slight the contact. They should be regarded as liable to become sources of infection at any time, and should not be allowed to go to school, nor to play with other children. If after the last possible time of exposure, fourteen days have elapsed without any cough having developed, it is safe to conclude that the child has escaped infection.

It is safest to regard the child with whooping-cough as a possible source of infection, as long as it still coughs. If, however, three months have elapsed, and if all the characteristics of the spasmodic

stage have disappeared, continued cough is not an indication for further isolation.

TREATMENT.—The treatment of whooping-cough is to be considered under four divisions, as follows: 1, General hygienic measures; 2, Internal and local treatment of the cough; 3, Treatment of special symptoms; 4, Specific treatment, or vaccine therapy.

GENERAL HYGIENIC MEASURES.—These are considered first, because they constitute the most effective means of influencing the severity of the disease. At least one-half of the cases of whooping-cough encountered in practice require no other means of treatment, and would even do better if no other measures were used. Much harm has been done by the indiscriminate prescribing of drugs in whooping-cough.

Fresh air stands at the head of the list of therapeutic measures in whooping-cough. The effect of being outdoors on the number and severity of the paroxysms is more obvious than that of any other means of treatment. Older children should go out every day even in winter, except on stormy, raw, or dusty days, and should be kept in the open air as much as possible. In the case of young infants and delicate children, some precautions must be taken. I believe, however, that even in winter these children should be taken out in their carriages on all fine days, but care must be taken to clothe them properly, and to guard them from raw damp weather, wind, dust, and sudden changes of temperature. When on account of weather conditions, patients cannot go out, they should be given indoor airings. Only those children who have fever, or are very sick, should be kept in bed, and even these should be put out on a porch or veranda in warm weather, or when weather conditions are favorable.

When children are indoors, more than one room should be used whenever possible, the patients being changed frequently from one well-aired room to another. The sleeping room should be arranged to admit plenty of fresh air. The least closeness of the atmosphere increases the number and severity of the attacks.

Change of climate has been highly recommended in whooping-cough. In infants I do not ordinarily recommend it, as the discomforts and limitations of hotel life are not good for infants, who do better at home. Change of climate is, however, useful in all cases in which during convalescence, cough is unduly prolonged. It is also beneficial to delicate patients in winter. A warm place near the sea-shore gives the most desirable climate.

The feeding of whooping-cough patients is important, and is sometimes difficult on account of the vomiting which accompanies the paroxysms. Whenever vomiting is a symptom, small meals, given more frequently, should be used. It is often necessary to depart

from the usual regularity of the feeding intervals, and to give the food shortly after a paroxysm, so that it will be retained as long as possible. In older children when vomiting is present, the diet should be fluid, chiefly milk, with some thin gruel or beef-juice. Even when vomiting is not prominent, it should be remembered that coarse, dry, solid food irritates the mucous membranes, and the diet should be confined to liquids and soft solids.

The nutrition of the infant is so easily affected that the utmost attention should be paid to the administration of the food. Small quantities of milk carefully modified to suit its digestion should be given at frequent intervals, preferably after the occurrence of a paroxysm, as it is then more likely to retain the milk in its stomach a sufficient length of time for absorption before the next attack. The amount of food which the infant retains in the twenty-four hours is an important factor in the treatment. In infants of from six to twelve months, at least 20 to 25 ounces of milk should be taken and retained in the twenty-four hours. When the amount is lessened to 12 or 15 ounces, the infant's nutrition, as a rule, suffers to such an extent that unless this amount can be increased, a fatal issue is likely to result. Under these circumstances, if the infant is not taking enough food, gavage should be resorted to. If the trouble is entirely the retaining of the food, gavage will sometimes help, as the tube is less apt to irritate the pharynx and precipitate a paroxysm than sucking. In desperate cases, some internal medication must be pushed till the paroxysms are lessened, but such cases are rare.

It is also important in whooping-cough to guard the child from every excessive stimulus to the nervous system. All forms of excitement, violent games, excessive noise and so forth, should be prevented.

INTERNAL AND LOCAL TREATMENT OF THE COUGH.—The drugs which have been recommended in the symptomatic treatment of the cough of pertussis are innumerable, and this fact is in itself an evidence that no one of them stands forth as of preëminent value. Whooping-cough is a disease of such irregular course, both as to number and severity of the paroxysms, that no man's judgment as to the efficacy of a therapeutic measure can be of much value. Each physician has his favorite remedies, which he believes to be the only ones of undoubted value, but which differ from those of other writers. I must confess to having no favorite drugs which I believe to be superior to others in whooping-cough. One drug seems to work better in one case, another in another.

I do not believe that drugs should be used as a routine in whooping-cough. Only when the number and severity of the paroxysms are so great as to reduce the strength of the child, to interfere with its nutrition, or to cause it obvious suffering, are drugs indicated.

The most effective drugs in controlling the paroxysms are the opiates, but owing to their other effects, they should only be used in cases of greatest severity.

When drugs are indicated, the physician should try one after another, keeping a careful record of the daily number of paroxysms. Two or three days suffice to test the working of a drug. When one is encountered which appears to produce an appreciably favorable effect, it is better to stick to it. The order in which the drugs are tried is arbitrary, and depends more or less on the fancy of the physician. In going over all the various text-book articles and recent publications, I have found that the drugs can be arranged in an order based on the preference of the majority.

On the basis of majority preference, *quinin* holds first rank in the early stages of whooping-cough. To infants the bisulphate should be given in aqueous solution, made up so that there is 1 grain to the teaspoonful for infants in the first year, and 2 grains to the teaspoonful for infants in the second year. A teaspoonful should be given three or four times a day. For older children the taste must be disguised, and the bisulphate may be given in syrup of sarsaparilla, orange, or yerba santa. The dose should be from 3 to 5 grains of the bisulphate according to the age, three times a day. In children over eight years, the sulphate may be given in capsules.

Antipyrin ranks next, and may be tried when quinin fails. The dose from six months to two years should be 1 grain every four hours, and this may be safely increased to every three hours, and then to every two hours, if no effect is produced. For a child from two to six years, 2 grains may be given every four hours, increasing to every two hours. After six years, 3 grains may be given. Antipyrin may be used alone, or combined with the bromides.

The bromides may be tried next. In the first year, bromide of sodium may be given in doses of 2 grains every four hours; in the second year, the dose may be 3 grains, and to older children 4 or 5 grains every four hours. Bromide of sodium may be given in combination with antipyrin.

Belladonna has been a favorite remedy for whooping-cough in the past. Present day opinion inclines to the belief that it is not often very effective. The dosage will be found in Division II, page 179.

It is admitted that the *opiates* are the most effective means of controlling the paroxysms, but owing to their other unfavorable effects, they should only be used in the severest cases, when other means fail.

Codein should be tried first, in the following doses: In the first year, $\frac{1}{8}$ grain; in the second year, $\frac{1}{8}$ to $\frac{1}{4}$ grain; from two to four years, $\frac{1}{8}$ to $\frac{1}{4}$ grain; from four to eight years, $\frac{1}{8}$ to $\frac{1}{4}$ grain; over eight years, $\frac{1}{4}$ grain. These doses should not be repeated

oftener than is necessary. Often a single dose at bedtime, sometimes repeated once later, suffices. No matter how severe the case, codein should not be given oftener than every four hours.

If codein fails, and the case is of the severest type, morphin should be tried, in the doses given in Division II, page 172

Bromoform sometimes works well as a substitute for the opiates. The dose should be from 1 to 5 drops three times a day according to the age of the child.

The *local applications* to the naso-pharynx, and the medicated sprays and inhalations which have been recommended in pertussis, are legion. In my experience neither local applications nor inhalations give the results claimed for them, and I have given up their routine use. For local applications to the naso-pharynx, the preparations most used are silver nitrate in 2 per cent solution, carbolic acid in 1 per cent solution, and resorcin in 1 per cent solution. For inhalations, creosote, carbolic acid, and cresolene are the favorites. The cresolene vaporizer in the room often has a soothing effect upon the child's parents, and can do no harm.

TREATMENT OF SPECIAL SYMPTOMS.—The only serious symptom in the average case of whooping-cough is the vomiting which accompanies the paroxysms, and which may seriously interfere with nutrition. The treatment of this is that of the general disease, and has already been considered.

The slight dilatation of the heart which often accompanies whooping-cough requires no special treatment, except that the children must be kept more quiet. Signs of real cardiac insufficiency are rare in uncomplicated cases and require rest in bed, and stimulation with caffein or digitalis, camphor being used in case of sudden collapse.

The ulcer at the frenum of the tongue is treated by protecting the teeth by a bit of adhesive plaster, and by the application of silver nitrate to the lesion.

The tendency to laryngospasmus and convulsions is best treated by the bromides, given in the same doses as are used in attempting to control the whooping-cough paroxysms. In all such cases, tests should be made for Chvostek's sign, the peroneal reflex, and increased electric excitability, in order to determine whether spasmophilia is the underlying cause of the symptoms. If this is the case, the treatment of spasmophilia should be added to that for pertussis.

Epistaxis is treated locally in the usual manner. The hemorrhages into the skin and conjunctiva require no special treatment. The serious hemorrhages involving the central nervous system are treated as described under cerebral hemorrhage. Mediastinal and subcutaneous emphysema have no special treatment, but if they produce serious symptoms, symptomatic stimulation is employed. The

albuminuria seen at times in pertussis also requires no special treatment.

The serious complications of bronchopneumonia and tuberculosis are treated as described under those diseases.

Prolonged cough in convalescence is treated as is chronic bronchitis, by means of tonics and change of climate.

SPECIFIC TREATMENT; VACCINE THERAPY.—Very soon after the establishment of the Bordet-Gengou bacillus as the presumable cause of whooping-cough, attention was turned to the possibility of a specific method of treatment. The long course of the disease, and the localized character of the lesions, suggested that vaccine therapy was the form of specific treatment most likely to prove of value. Vaccines prepared from cultures of the whooping-cough bacillus were placed upon the market, and have been very widely employed. Recent medical literature is filled with innumerable reports on the results of vaccine treatment in whooping-cough. The majority of these reports are favorable. Some observers believe that the use of the vaccine not only lessens the number and severity of the paroxysms, but also shortens the course of the disease and tends to prevent complications. Other observers are not so sanguine as to the shortening of the course of the disease and the prevention of complications, but believe that the number and severity of the paroxysms are favorably influenced. One encounters many "pleas for the more extended use of vaccine therapy in whooping-cough."

These reports are by no means convincing. It is extremely difficult to estimate the value of any therapeutic measure in a disease so irregular in its clinical manifestations as is whooping-cough. The history of therapeutic endeavor clearly shows that most means of treatment, the results of which are estimated by their effect upon clinical symptoms, are held as effective when first tried. Our minds unconsciously tend to see favorable results from our therapeutic endeavors. The investigators whom one would naturally select as being men having the most critical and impartial minds, have published reports unfavorable to the value of the vaccine in pertussis.

I note a report by Hess of an epidemic of whooping-cough in which four different vaccines were used, including an autogenous vaccine. No one of them showed any effects of value in curing or modifying the disease in this epidemic, in spite of the fact that many cases received early inoculations, or even prophylactic inoculations.

Vaccine therapy in the treatment of pertussis is possibly worthy of further trial. It has been established that it does no harm, and it can be used in any case in addition to the ordinary methods of treatment. The usual dosage is from 100,000,000 to 300,000,000 bacteria, given every other day.

Even if the whooping-cough vaccine has no therapeutic value, it may have some value in prophylaxis. Some writers believe that its prophylactic value has been adequately proven. In Hess' report, twenty children developed whooping-cough in spite of prophylactic inoculation. On the other hand, a greater percentage of cases developed among the unvaccinated than among the vaccinated.

My own present practice is to use prophylactic vaccines in cases known to have been exposed to whooping-cough, and therapeutic inoculation in cases which are running a severe course. I do not, however, allow vaccine therapy to replace other therapeutic measures.

PROBLEMS AND RESEARCH.—The chief problem awaiting final solution has already been discussed, namely, the value of vaccines in the treatment and prophylaxis of whooping-cough. It does not seem likely that conclusive proof will be attained in the matter of vaccine therapy, but the value of vaccine prophylaxis will probably be settled in a comparatively short time.

Considerable work remains to be done in the study of the Bordet-Gengou bacillus and its biological reactions. It is yet to be determined whether the organism represents one or several types or strains. The constancy of the complement fixation test must also be proven more conclusively. Positive tests have been obtained by using the Noguchi hemolytic system, the antigen being prepared from a pure culture of the Bordet-Gengou bacillus grown in ascites-fluid agar. It is possible also that future research will throw more light upon toxin formation and the nature of the antibodies.

New suggestions as to internal and local remedies will probably continue to appear from time to time. Adrenalin has recently been suggested as of value in controlling the paroxysms.

MUMPS

(Epidemic Parotitis)

Mumps is a contagious disease of which the chief symptom is usually an acute swelling of the parotid gland. The disease is undoubtedly a specific infection, as is shown by its marked transmissibility, and its tendency to occur in smaller or larger epidemics. These epidemics are particularly likely to occur in schools and institutions.

ETIOLOGY. THE MICROORGANISM.—The organism which causes mumps is unknown. It is probably a filterable virus like that of poliomyelitis. Like other diseases of this class, mumps is characterized by a lymphocytosis.

TRANSMISSION.—Mumps is transmitted directly from an infected individual to a healthy person. The virus can be carried over by healthy persons and on contaminated objects. It is not known

whether actual contact with infected material is requisite, or whether the virus can cross an air-space. In my opinion it is probable that the contagium is not air-borne. It is usually assumed that the virus enters through the mouth, and reaches the parotid gland through Stenson's duct. In view of the occasional localization of the disease in places other than the parotid gland, this must be regarded as questionable.

The contagious period of mumps begins with the first appearance of symptoms, and according to some observers, the disease may be transmitted one or two days before the appearance of swelling of the parotid. The duration of the contagious period is not definitely known, and is probably variable. The infectivity probably ordinarily ceases rapidly during convalescence, but has been known to persist for one or two weeks. The spread of the disease is favored by the frequent occurrence of mild ambulant cases.

PREDISPOSITION.—Some writers state that the susceptibility to mumps is not very great. This I believe to be a careless statement. It is based on the fact that mumps only occurs in a small percentage of those exposed. As the mode of transmission is not thoroughly known, it is impossible to say what constitutes exposure. In scarlet fever only a small percentage of the exposed are infected, and this is known to be due not to a varying susceptibility to scarlet fever, but to the fact that the virus of scarlet fever is not air-borne, and that actual contact with infected material is essential for transmission. In mumps the mode of transmission is probably similar to that of scarlet fever, and accounts for the apparent relative insusceptibility.

Mumps is most common between the ages of five and fifteen years. The disease is very uncommon in infants under two years, although rare cases have been described even in the newborn.

IMMUNITY.—An attack of mumps confers a long-lasting immunity. Owing to the doubt as to the exact mode of transmission, it is impossible to say with certainty how long this immunity lasts, as adults are probably much less frequently exposed than children. Second attacks do not occur in childhood, but in adults are relatively rather more common than with the exanthemata.

INCUBATION.—The incubation is very long, averaging from seventeen to twenty-one days. Family epidemics are consequently often long drawn-out.

PATHOLOGICAL ANATOMY.—Opportunities for pathological examination of the tissues involved in mumps have been very rare. The process appears to consist of edema and congestion in the interstitial tissue of the parotid, and of the tissues adjoining the parotid, accompanied by a certain amount of round cell infiltration. The parenchyma of the gland does not appear to be involved.

In the majority of cases the parotids alone are involved. At times, however, similar changes take place in the other salivary glands. In a certain number of cases, chiefly occurring among adolescents or adults, there is an *orchitis* which is usually classed as a complication, but which is probably rather an unusual localization of the mumps infection. The pathological process is an interstitial inflammation of the body of the testicle, not affecting the epididymis. While the parenchyma of the testicle is not involved in the inflammatory process, the interstitial inflammation may be followed by atrophy of the testicle.

In females, a similar accompanying interstitial inflammation of the ovaries, breasts, or labia majora has been observed. Instances of such a localization of the process are extremely rare, but most of them have been seen in children.

SYMPTOMS.—While there are probably general prodromal symptoms in all cases, they do not attract attention in the milder attacks, and often the first thing to be noticed is the beginning of local symptoms. In the severer cases, the prodromal symptoms are often marked, and last from twelve to thirty-six hours before the appearance of local pain or swelling.

The usual prodromal symptoms are weakness, malaise, anorexia, chilly sensations and fever. The initial fever in mild cases is about 100° F. or 101° F. In severer cases there may be headache, vomiting, pain in the back and limbs, profuse sweating, and a temperature of 102° to 104° F. Nosebleed has been seen in the prodromal stage, and even convulsions have been reported.

The first local symptom is usually pain, which is referred to the area just below the lobe of the ear, and which is increased by movement of the jaws, and sometimes by the presence of sour substances in the mouth. Swelling of the parotid appears soon after, or sometimes simultaneously with the pain. Over the site of the parotid behind the ramus of the jaw appears an indefinite thickening, which is often at first more apparent to the eye than to palpation, and which is best observed by comparing the two sides. Occasionally both sides are affected simultaneously, but usually the involvement of one side precedes that of the other by several days. The swelling increases, feels tense and doughy on palpation, and has no sharply defined boundaries. The size reached by the swelling varies with the severity of the case; in marked cases the tumor may fill the lateral region of the neck between the jaw and the sterno-mastoid muscle, and may extend up on the face as far as the zygomatic arch. The essential feature in diagnosis is the presence of swelling, immediately under the lobe of the ear, and in front of the tragus.

Pressure over the swelling in the majority of cases is slightly dis-

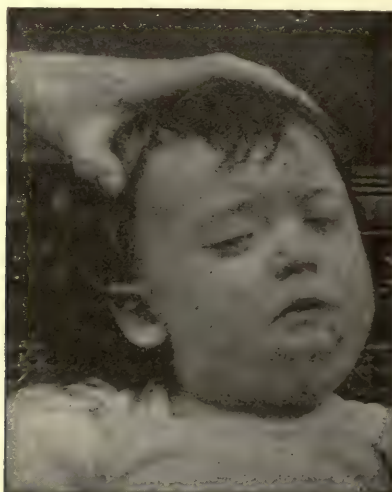
agreeable rather than painful, though occasionally the tumor is more sensitive.

During the height of the swelling, there is a tense sensation over the side of the face, opening the mouth is difficult, and chewing painful. Pressure on the external auditory meatus may produce slight deafness.

The swelling increases in size for two or three days after its appearance, remains stationary for two or three days more, then rapidly subsides. Usually both parotids are involved, but occasionally only one is affected. The interval between the swelling of the two sides is usually only two or three days, but occasionally may be a week or more.

The mucous membrane of the mouth and throat often shows a slight reddening in mumps, but more severe inflammation is very rare. The salivary secretion shows no notable changes, except that in some cases its amount is increased.

FIG. 140



Submaxillary mumps

The fever follows no regular course. The temperature falls with the disappearance of the swelling, and is likely to rise again when the second gland becomes involved. Often the fever is so moderate and of such brief duration that it passes unnoticed.

The blood shows a slight increase in the total white count, due to a relative and absolute lymphocytosis, which is clearly apparent in the differential count.

In a small proportion of cases the other salivary glands are involved. The submaxillary glands are affected oftener than the sublingual. The swelling of the submaxillary glands may occur simultaneously

with that of the parotids, or a few days later. Occasionally the submaxillary glands alone are affected, and in such cases the diagnosis is difficult unless there be an existent epidemic or a recognized exposure.

The entire duration of mumps is from five to seven days when only one side is affected, but may extend to ten or twelve days when both sides are affected. Constitutional symptoms usually persist only from three to five days. Relapses are extremely rare. The majority of cases in children run a mild course, as described, without severe symptoms.

COMPLICATIONS AND SEQUELAE.—In childhood complications are rare and comparatively unimportant. In adolescence and in adult life more severe complications are seen.

Orchitis is usually described as a complication of mumps, but is really an unusual localization of the specific infection. It is extremely rare in childhood, there being very few instances under the age of fifteen years, and practically none under the age of twelve years. After the fifteenth year, orchitis is seen in about a third of the cases of mumps. It occurs most commonly about a week after the beginning of the parotitis, usually not until the parotid swelling has subsided. The onset is ordinarily attended by high fever and severe constitutional disturbance, which is accompanied or followed by a painful inflammatory swelling of one or both testicles. After the decline of the inflammation, there may be an atrophy of the testicles which, when both sides are involved, may produce sterility. Occasionally the orchitis may precede the parotitis, and exceptionally it may be the only manifestation.

In girls, a painful swelling of the ovaries and breasts is occasionally seen. This is rare at all ages, but may occur in childhood.

Nephritis is occasionally seen after mumps, as after other infectious diseases. It is usually of a hemorrhagic type, and is only transitory.

The Nervous System is sometimes affected in mumps, more often in adults than in children. Such sequelae are rare, but are perhaps commoner than any others. The group of symptoms suggesting meningeal irritation which are often conveniently described under the term "meningismus," are sometimes seen during or following an attack of mumps. These vary much in severity. At times there is only headache, apathy, and slowing of the pulse, and lumbar puncture shows only an increase in the quantity and pressure of the cerebrospinal fluid. In rare cases there may be more severe symptoms, with rigidity of the neck, Kernig's sign, delirium, and temporary local spasm or paralysis. In these cases the cerebrospinal fluid shows not only an increase in quantity and pressure, but an increase

in the cell count. The symptoms are due to a toxic irritation of the meninges, and the process is that described by European writers as serous meningitis. The prognosis is favorable, except in the rare cases when there is an actual encephalitis.

Multiple neuritis is seen at times. Transitory facial paralysis from pressure of the parotid tumor has been observed. There are other rare complications caused by a sudden acute inflammation of the auditory labyrinth, which leads to permanent deafness. Otitis media is comparatively rare in mumps.

Suppuration of the parotid gland as the result of secondary infection has been observed in mumps, but is a very uncommon complication.

DIAGNOSIS.—The diagnosis of mumps is usually easy, and often does not require the special knowledge of a physician. Except for rare metastatic inflammation in certain severe infections, practically no other condition causes an acute swelling of the parotid glands, and in doubtful cases the diagnosis depends upon recognizing that the swelling involves the parotid rather than some other tissue. The conditions most often confounded with mumps are acute *cervical lymphadenitis*, and *alveolar abscess*. In the former condition the tumor is usually entirely below the ear, and behind the jaw, and is smaller and more sharply defined if only a single lymph node is involved. If the lymphadenitis involves a mass of nodes, the separate nodes are usually palpable, or else painful very tender phlegmonous inflammation is evident. In alveolar abscess the connection of the swelling with the jaw can usually be made out. In mumps the swelling is doughy, not sharply defined, not reddened, not acutely tender, and occupies the region immediately in front of the tragus.

Metastatic inflammation of the parotid glands is seen only in the course of severe infections such as diphtheria and typhoid fever, and the process early inclines toward suppuration.

Mumps confined to the submaxillary glands or to the testicles, cannot be diagnosed with certainty except in epidemics, or with a history of definite exposure.

PROGNOSIS.—In children the prognosis is very favorable. Complications are rare and mild, and the great majority of cases terminate in a few days in complete recovery. In children approaching adolescence, unfavorable complications occasionally occur.

PROPHYLAXIS.—In spite of the mildness of the disease, cases of mumps should be isolated whenever there is any possibility of contact with susceptible persons. Children in schools or institutions should be quarantined for three weeks.

TREATMENT.—There is no specific treatment for mumps, and the disease being brief and self-limited, none is needed. The symptoms are so few and so little distressing, that no symptomatic treatment is required. Children should be kept in bed during the period of fever and constitutional symptoms, and should be kept in the house until the glandular swelling has disappeared. The diet should be fluid as long as there is any pain on mastication. The swollen gland may be protected by a pad of soft cotton. If pain is severe, heat may be applied, either with a hot water bag, or by an inunction of warm olive oil. Alkaline mouth washes should be used frequently. Complications should be treated according to their symptomatic indications.

PROBLEMS AND RESEARCH.—The central problem in mumps is the discovery of the organism which causes the disease. A certain amount of analogy with other diseases in which there is strong evidence that the cause is an ultramicroscopic filterable virus, suggests that mumps belongs also in this class. The first step in the investigation of the etiology of such infections is the reproduction of the disease in animals. Such attempts have been made in mumps with filtered saliva, but up to the present time the results of these investigations remain very incomplete. A transitory tumor of the parotid has been produced in monkeys with filtered saliva, but not constantly, so that it is possible that the tumor may represent some secondary infection.

Hess has been working on the production of artificial immunity by injecting exposed children with the blood of immunes. The quantity of blood obtained is 6 to 8 c.c., and this, injected intramuscularly, causes no unfavorable reaction. This procedure is promising in mumps, as the long period of incubation permits inoculation some time after exposure. In Hess' cases, mumps did not develop in any exposed child thus inoculated.

The blood changes in mumps have been thoroughly studied. It has been found that the lymphocytosis begins on the first day, and persists for fourteen days. It is believed that these changes may prove of value in the differential diagnosis from lymphadenitis. Feiling has found an increase of lymphocytes in the cerebrospinal fluid in cases which did not show meningeal symptoms.

INFLUENZA

(La grippe)

In the strictest sense, influenza or la grippe is an infectious and highly contagious disease, due to the *bacillus influenzae* and occurring generally in epidemics.

In 1889 a great epidemic of influenza appeared, apparently coming out of Asia, spreading over the whole of Europe, and crossing to the United States. This was really a pandemic. The disease in this country reached its height in 1891. Since this great pandemic the disease has appeared sporadically every winter with greater or less severity.

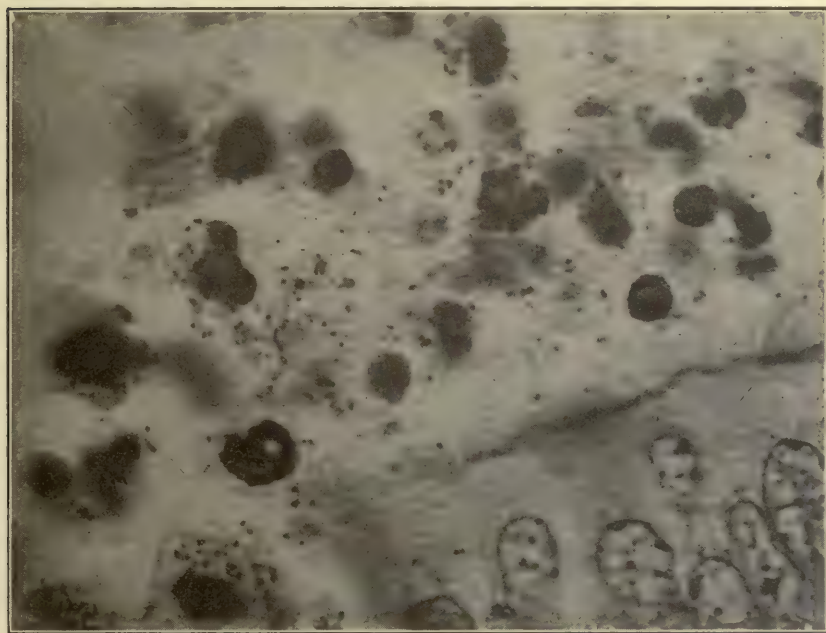
The existence of such a widespread pandemic afforded excellent opportunity for bacteriological study of the disease, and R. Pfeiffer discovered the bacillus which has been generally accepted as the specific cause of the disease. The great epidemic of 1891 also afforded opportunity for a study of the clinical picture of influenza, and the classical description of the disease dates from that epoch. Since the years of the epidemic, however, the term *grippe* has gradually come to be more and more loosely used. There is no doubt that various other infections of the respiratory tract, usually of a mixed etiology, can give the same clinical picture as is characteristic of epidemic influenza. The term *grippe* as ordinarily used both by layman and physician, is applied to the description of a definite clinical picture without reference to the bacteriological etiology. Of the cases thus described as *grippe*, some are undoubtedly true instances of sporadic infection with Pfeiffer's bacillus. Nevertheless the majority of cases which each winter are called *grippe* are not instances of true influenzal infection, but are simply ordinary mixed infections of the respiratory tract with constitutional symptoms of unusual severity.

As a result of this confused relation between bacteriological etiology and symptoms, a distinction has been made by some writers between the terms *influenza* and *grippe*, the former being applied only to the disease actually caused by Pfeiffer's bacillus and usually appearing in epidemics, the latter being applied to cases with similar symptoms but of different etiology. *Grippe*, however, has usually been regarded as a synonym for true epidemic influenza, and, I believe that to apply it to cases which have a different etiology would only increase the confusion. On the other hand, the average layman is so thoroughly satisfied with the term *grippe*—as used in the diagnosis of his symptoms—that he cares little for bacteriological etiology. The physician, however, when he uses this term, should be clear in his own mind whether he means actual infection with the bacillus of influenza, or whether he means a common cold with *grippe*-like clinical manifestations.

ETIOLOGY. THE MICROORGANISM.—The bacillus *influenzae* or Pfeiffer's bacillus, is an extremely minute organism, irregular in length, with rounded ends. It is Gram-negative and can be stained with the ordinary stains, showing particularly well with dilute carbol-

fuchsin. In the sputum it appears as a very minute bacillus, which on account of the bipolar staining often resembles a minute diplococcus. The bacilli when present in the sputum, and when the cause of the infection, are usually very numerous and occur in large clumps or masses. In cultures the organism is aerobic, and grows best on blood-agar, on which it appears as minute colorless droplet colonies. It grows only on media containing hemoglobin, this being the most important point in its differentiation from other microorganisms of similar morphology.

FIG. 141



Influenza bacilli in the sputum

The organism is found usually in the sputum from the lower air-passages. It is found less frequently in the discharges of the nasopharynx, and in the discharge of acute otitis. Still more rarely it is found in the pus of empyema and in the cerebrospinal fluid.

TRANSMISSION.—The disease is transmitted precisely in the same way as in whooping-cough and measles, by “droplet infection.” It is thus an air-borne contagion, and it is necessary for the individual to be infected to come into the actual presence of the one already infected. There is no evidence that the disease can be carried upon contaminated objects.

PREDISPOSITION.—At the time of the epidemic almost the entire population was attacked. There did not, however, appear to be

much evidence that immunity was afforded by an attack, because during the epidemic recurrences and second attacks were not uncommon. In the sporadic cases which have occurred each winter since the pandemic of 1891, the predisposition to the disease is evidently much lessened, as only a small proportion of the population are attacked by true influenza. Whether this is due to a partial immunity conferred on the population during the epidemic, or whether it is due to a lessened virulence of the infecting organism, is not known.

Influenza may occur at all ages, but is much commoner in adults and older children than among young children. Infants are comparatively infrequently affected, even in epidemics, and younger children usually have the disease in a mild form.

The disease is usually seen in the winter and spring months, disappearing with the advent of warm weather.

The incubation period is not definitely known. It is usually short, probably not more than four days.

PATHOLOGICAL ANATOMY.—The lesions produced by the bacillus of influenza show nothing particularly characteristic of the disease. The inflammation of the upper air-passages and of the bronchi is of a catarrhal character. In the lower respiratory tract the disease often spreads to the smaller bronchioles and lung tissue, resulting in bronchopneumonia. Influenza meningitis occurs at times, but it is comparatively rare.

SYMPTOMS.—The onset of influenza is usually very acute, and the symptoms are variable. At times they are the same in children as in adults, but in infants and young children the symptoms are often not so severe as in the adult, although they vary in different epidemics. It is a characteristic of epidemic influenza that it has no distinct group of symptoms of its own. The symptoms are chiefly a catarrhal affection of the nose and throat, and frequently of the bronchi. These symptoms in young children are accompanied evidently by great discomfort, at times amounting to pain, in the limbs and body, although on account of the age of the patient it is often impossible to determine whether much pain is present. Sometimes the only marked symptom is a heightened and irregular temperature, with marked apathy, and the disease may be so mild as to be recognizable only during an epidemic. In older children the symptoms, although as a rule not of so severe a type as in adults, are at times quite serious, especially if continuous vomiting occurs. Severe headache and delirium are present in some cases, as well as extreme emaciation, out of proportion to the fever or to the morbid conditions detected on physical examination. Severe symptoms connected with the larynx and the lungs may also arise and rapidly disappear.

In young infants, even when no complications arise, the apathy and prostration may become extreme, and death may take place seemingly from the overwhelming intensity of the infection.

There is a tendency to the development of tuberculosis after influenza. Relapses and recurrent attacks are not uncommon. Out of a large number of cases in children examined by Schlossmann, albuminuria occurred in 8 per cent, but nephritis was rare. Anemia is a common sequela in young children. Leukocytosis in uncomplicated influenza is not present. The mental disturbances and multiple neuritis so common in adults are not marked sequelae in children.

VARIATION IN TYPE OF THE DISEASE.—It is now generally recognized that there are distinct types of the disease.

RESPIRATORY TYPE.—In this, the most common form of the disease, the influenza bacillus may attack any part of the respiratory tract from the nose to the pulmonary alveoli, the symptoms increasing in severity according as the latter are approached. In the milder forms there are the usual symptoms of acute coryza, fever, and headache, but these symptoms are accompanied by a far greater degree of prostration than is met with in ordinary attacks of catarrhal rhinitis. The milder cases, without complications, may last only a few days; the temperature is usually moderate— 101° to 103° F., but the prostration is marked. An annoying, persistent cough is commonly present.

This form is sometimes much intensified, may last longer, have a higher temperature, and show a greater tendency to complications, especially in the development of otitis media and cervical adenitis.

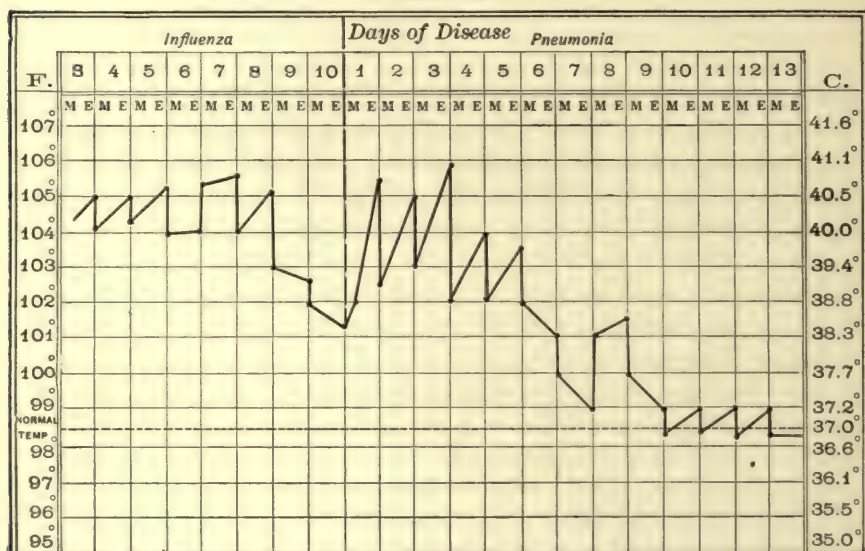
In another set of cases of the pulmonary type, the disease, instead of retrograding steadily, progresses, and with the development of bronchitis, delirium, and extreme prostration, may simulate typhoid. The bronchitis has no especial peculiarities, but in young children it assumes at times a very intense grade, reaching the finer bronchi and producing cyanosis and threatened asphyxia.

In certain instances an influenza pneumonia develops. This pneumonia is usually lobular. Generally, there are small areas of bronchopneumonia diffusely scattered, and often giving rise to no other physical signs than patches of moist râles. The sputum in these cases of influenza bronchopneumonia is never "rusty," but is purulent and generally of a greenish-yellow color. A diagnosis can be made by finding the influenza bacilli in the sputum in large numbers within the polynuclear leukocytes. The resolution of such a pneumonia is prolonged, ending by lysis. This class of cases is very serious, and much of the mortality of epidemic influenza arises from these pulmonary complications.

Pleuritis may occur in the course of influenza, but is rather rare; when present, however, it is apt to become an empyema.

NERVOUS TYPE.—In certain cases catarrhal symptoms are slight but nervous symptoms are prominent. Pains in all parts of the body and limbs, cerebral symptoms simulating meningitis, convulsions, delirium, opisthotonos, symptoms simulating pneumonia without, however, the physical signs of that disease, or a typhoid condition with weak, rapid pulse, a temperature of 105° to 106° F., and irregularity of the heart, are seen. All these severe and alarming symptoms usually pass off in two or three days and leave no trace of any of the simulated diseases, although the resulting prostration may last for a long period.

CHART 14



Epidemic influenza. Pneumonia. Recovery. Male, 16 months old

GASTRO-ENTERIC TYPE.—In this form of the disease the prominent symptoms are nausea, vomiting, abdominal pain, diarrhea and a tendency to collapse.

The spleen is enlarged in a certain number of cases, and this, according to Osler, depends on the intensity of the fever. These symptoms may last only two or three days, and, as a rule, are not followed by an unfavorable result.

FEBRILE TYPE.—The temperature in influenza is very variable, and, as stated by Osler, may, with its accompanying prostration, be the only manifestation of the disease.

It may be remittent and associated with chills, or, on the other hand, may be of a continued type, and so prolonged as to simulate typhoid fever.

DIAGNOSIS.—If the term gripe be applied to a case which shows a symptom-complex in any way resembling the above description, the physician must remember that the use of the term does not imply that the case is actually one of infection with the bacillus of influenza. The diagnosis can only be made by the finding of the specific organism in the sputum. Furthermore, the organism should appear in the sputum in such large numbers as to be unmistakable, and in a case of influenza bronchopneumonia, clumps of the organisms should be found within the leukocytes. The technic of the examination of the sputum has been described in Division II. Although the appearances found in the sputum are often strongly suggestive, positive proof of the identity of the organism can only be obtained by demonstrating that it will grow only upon a hemoglobin-containing culture medium.

TREATMENT.—At the present time there is no generally available specific treatment for the disease, and the treatment must be symptomatic. The general lines of treatment are those of any acute contagious disease. It is best to isolate the patient during the attack under the same precautions as are employed in other air-borne contagions, and it is desirable to fumigate the sick room after the disease is over.

Children with influenza should be kept in bed and be treated as in any acute infection. The bowels should be opened at the onset of the disease with calomel or castor oil. High fever is best controlled by cold sponging or the cold pack. Nervous or subjective symptoms are treated with small doses of phenacetine. Codein may be added if pain is very severe. When there is severe and continuous vomiting, small doses of iced champagne by mouth, and enemata of bromide of potassium are indicated. Stimulation is occasionally needed when the pulse shows signs of weakness, and is administered as in the other acute infections. When the convalescence is prolonged, especially if there be a tendency to prolonged cough, a change of climate is very advantageous.

SERUM THERAPY.—Work has been done at the Rockefeller Institute in the preparation of an anti-influenza serum. Up to the present time this serum has only been employed in cases of influenza meningitis. The comparative rarity of cases which are adequately proven to be true influenzal infections of the respiratory tract, has made it impossible as yet to test the value of serum therapy against this form of influenza infection. We shall have to await another wide spread epidemic before we can test the value of serum therapy.

III. DISEASES WITH CONSTANT INFECTION OF THE BLOOD

TYPHOID FEVER

Typhoid fever is an acute infectious disease, characterized by specific lesions mainly involving the intestine and its lymphatic apparatus, and by a clinical picture in which general toxic symptoms predominate. Unlike the highly contagious diseases included in the groups considered above, typhoid fever is not especially a disease of childhood. For an exhaustive description of the disease the reader is referred to text-books on general medicine. Only the peculiar modifications of the disease seen in childhood will be thoroughly considered here.

ETIOLOGY. THE MICROÖRGANISM.—Typhoid fever is caused by a specific microörganism, usually spoken of as the typhoid bacillus (bacillus of Eberth). This bacillus resembles the organisms of the so-called colon group. From the beginning of the disease and throughout the febrile period, the bacillus is constantly present in the specific lesions of the disease, and in the blood. The organism is to be found in the stools and urine not only during the febrile period, but for a varying period during convalescence. Healthy carriers of typhoid bacilli, in whom the organisms persist a long time after recovery, have been found among children, but are much less common than among adults. The infrequency of youthful carriers is due to the fact that the gall bladder is rarely involved in childhood, and it is mainly in the gall bladder that the bacilli of carriers persist.

TRANSMISSION.—The transmission of typhoid, especially in childhood, is much more often direct than is generally supposed. The habitual uncleanness of young children favors the infection of persons who are in intimate contact with them. The carrying over of the disease occurs almost exclusively through the bacilli which are excreted in the urine and feces, and which find an opportunity to contaminate objects, drinking water and food. The typhoid bacillus under favorable conditions maintains its life and virulence for a long time outside the body. Contaminated objects are handled by others, and the bacilli conveyed to the mouth. Through the contamination of drinking water and milk supplies, widespread epidemics are brought about. The bacillus always finds its entrance through the mouth. The cases in which the breast-fed infants of mothers with typhoid contract the disease are to be explained, not by passage of the typhoid

bacilli through the mammary gland, but by the contamination of some object which comes in contact with the child's mouth through uncleanness. The breast-fed infants of typhoidal mothers often remain healthy.

Typhoid fever is, through the conditions of its transmission, extremely likely to affect more than one member of a family.

PREDISPOSITION.—After the fifth year, the frequency of occurrence of typhoid fever is about the same in children as in adults. In children from two to five years of age typhoid is much less frequent than later. In infants under two years, typhoid is rare, especially in the first six months, when it is very exceptional. It should be remembered that typhoid can occur in infants, although it is uncommon. It is possible also that some cases of typhoid in infancy are overlooked on account of the atypical clinical picture presented. Congenital typhoid is not uncommon in children born of mothers sick with the disease. In such cases the bacilli gain entrance to the fetal circulation through the placenta. The commonest result of fetal infection is death of the fetus and abortion, but a child may be born alive with typhoid, and die soon afterward on account of its feeble resistance.

The susceptibility to typhoid fever is general, and there is no definite evidence of variations in susceptibility or of relative immunity, even in infancy. The smaller frequency of the disease in infancy is probably to be attributed to the fact that infants have less opportunity to come into adequate contact with infected material.

IMMUNITY.—Although typhoid fever is a self-limited disease, it is probable that the immunity following an attack lasts only for a brief period. Several attacks are comparatively common.

PATHOLOGICAL ANATOMY.—In childhood the pathological lesions are less definite in indirect ratio to the age. After the second or third years the lesions are constant and the pathology definite. Although the more advanced and severe lesions of typhoid fever may occur in the early as well as in the later years of life, yet its characteristic lesions in young subjects are found to be less definitely pronounced. They consist essentially of a hyperplasia of the solitary lymph-follicles and Peyer's patches, and the process, instead of going on to ulceration, usually terminates in early resolution with fatty degeneration of the cells. Ulceration is absent or slight, and hemorrhage and perforation are therefore rare complications in the typhoid fever of early life.

In addition to the lesions in the intestine, hyperplasia of the mesenteric glands, granular degeneration of the liver and kidney, and granular or fatty degeneration of the heart may be found. Parenchymatous changes sometimes occur in the peripheral nerves, with

degeneration of the muscles. The pathological conditions in typhoid fever in the early years of life may be said to correspond with those which are met with in the aborted forms of the disease in later life.

FIG. 142



Typhoidal ileo-colitis, showing ulcers of colon. Female, 2 years old

The specific efflorescence of typhoid fever, the rose-spots, have acquired additional importance in the diagnosis from recent bacteriological investigations. Various observers have demonstrated the presence of the typhoid bacillus in the rose-spots in a very large proportion of the cases examined.

SYMPTOMS.—The typical clinical picture of typhoid fever in children differs markedly from that seen in adults. This applies to the general run of cases. It must be remembered, however, that instances are frequently encountered in which the disease runs a course in every way resembling that characteristic of adult typhoid, and every variation in symptomatology and severity which are encountered in adults may occasionally be seen in children. It will be assumed here that the reader is thoroughly familiar with the general description of typhoid fever, which is that of adults, and attention will be mainly devoted to pointing out the differences characteristic of the disease as most frequently encountered in childhood.

THE USUAL CLINICAL PICTURE IN CHILDREN

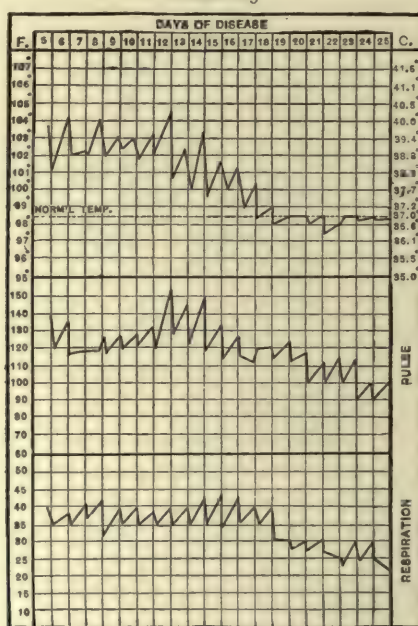
Typical typhoid fever in childhood resembles more or less the mild cases of the disease as seen in adults. Its principal peculiarities are the following: A shorter febrile period with greater frequency of abortive forms; a less high range of temperature; absence of the severe toxic manifestations of the disease affecting the nervous system; infrequency of complications, particularly hemorrhage and perforation.

THE ONSET.—In typical cases the child becomes ill with rather vague symptoms, but the onset, while not sudden, is rather more definitely marked than is often the case in adults. The symptoms in this prodromal stage are weakness—the child tiring easily—loss of appetite, restless sleep, and at times occasional vomiting. In older children there may be headache, which is usually not very severe. Epistaxis is very rare. In this stage high fever is usually found, or the temperature is becoming higher each day, and one of the points which especially attracts the attention is that the most careful physical examination fails to reveal a cause for the temperature, which is high in proportion to the general constitutional disturbance. In many cases the constitutional disturbance is so slight that it is only the fever which attracts attention.

THE FEVER.—The temperature curve in childhood bears a general resemblance to the classical curve of adults. There is a period of step-like rise of temperature, a period of high continuous fever, a period with marked daily remissions, and a period of fall by lysis. In children, however, all these periods are apt to be shorter, the entire course of the disease being more compressed. The temperature

usually reaches its maximum by the fourth or fifth day, and sometimes even before. It is not uncommon for the step-like rise of temperature to be absent entirely and for high fever to be present on the very first day. It is difficult however in such cases to date the beginning of the illness, and it is possible that the beginning of the fever has been overlooked by the parents. The stage of high continuous fever is shorter, and characterized by greater remissions, and there is no definite remittent stage, so that the whole period during which the temperature remains at its height may not be more than a week. Lysis occupies only from three to five days. In typical cases the entire febrile period is from two to three weeks. In children under

CHART 15



Typhoid fever. Male, 5 years old

five years the temperature often does not go above 103° or 104° at any time, while in older children a higher range of temperature is more common, but not so common as in adults.

GENERAL SYMPTOMS.—During the first week the diagnosis of typhoid fever is usually very uncertain, only the high fever without definite cause suggesting typhoid. General symptoms are not marked. There may be occasional vomiting, and in older children some headache, but in general weakness, apathy, and loss of appetite are all that are noted. The *tongue* is usually dry and heavily coated; in older children it is often clean at the tip and sides. The dryness and coating of the tongue, however, rarely reach so high a grade as

in adults. The lips are often dry and cracked, and children are very apt to pick them. The *spleen* is usually palpable below the costal border at the end of the first or beginning of the second week. With careful examination the splenic tumor should be found in the second week in every case, but after the second week the spleen is usually not to be felt. The *rose-spots* appear usually at the beginning of the second week. In children rose-spots are usually very sparsely scattered, and are often to be found only upon the abdomen after careful search. In the younger children they are often absent entirely, and in general rose-spots are less constant than in adults, appearing in not more than 60 to 70 per cent of the cases. *Abdominal distention* is much less common in children than in adults and is seen most often in older children. Even when present, it is usually less obstinate and less apt to require treatment than in adults. Pain and tenderness of the abdomen are unusual, although some children complain of pain on pressure over the appendix region, but do not show involuntary muscular spasm. *The bowels* in the typhoid fever of children show much less characteristic disturbance than in adults. In general constipation is more common than diarrhea, and this is particularly true in the younger children. Diarrhea however is seen at times, especially in the severer cases. The stools, even when diarrhea is present, are not so characteristic in appearance as in adults, the typical pea-soup stool being rare. *Bronchitis* of a mild form is present in the majority of cases, especially in children of weak constitution. Occasionally the bronchitis is so marked as to lead to an error in diagnosis, the physician being led to believe that the infection is chiefly located in the lungs. In weak and rachitic infants, bronchopneumonia may develop. *The circulation* in typical cases of typhoid fever in early life is much less disturbed than in adult life. The pulse and heart sounds do not usually show signs of weakness sufficient to require stimulation. The relative slowing of the pulse in proportion to the height of the fever which is so important a diagnostic sign in the typhoid fever of adults, does not appear in children until after the sixth or eighth year; and the same is true of the dicrotic pulse. *The nervous system* is much less affected in children than in adults. The more severe nervous symptoms so pronounced in later life are not prominent in early childhood. Headache of a mild type is not uncommon, especially in the early stage of the disease; severe headache is very uncommon. Crying out at night, especially in young children, and delirium of a mild type are not uncommon. Deep stupor is rare; in fact the chief characteristic of typhoid fever in young children is apathy. The child takes the nourishment which is given to it, is not especially restless, and usually lies in a half-somnolent condition. *The urine* often shows a small amount of albumin and a few casts and blood corpuscles, especially in cases with high fever.

The diazo reaction usually appears at the end of the first week and persists during the febrile period. *The blood* shows a pronounced leukopenia, the white count often falling to half the normal for that age, or even less. The neutrophiles are proportionately more diminished than the basophiles, and the eosinophiles disappear entirely.

CONVALESCENCE.—The length of the febrile period in typical cases in children is only from one and one-half to three weeks, and after three or four weeks the children are usually in full convalescence and recover their full strength more rapidly than do adults.

THE SEVERE FORM IN CHILDREN

Severe cases resembling the typhoid fever of adults are seen most often in the later years of childhood. In such cases the fever is higher the course is longer, subjective symptoms of all kinds are more marked, and apathy is so pronounced as to become somnolence or coma. Food is often refused entirely, the pulse becomes rapid, compressible, and of small volume and cough is often severe. Diarrhea is often marked in such cases, and either hemorrhage or perforation is sometimes seen.

The symptoms of severe cases which are most characteristic of childhood and which are not seen in adults, are those of meningismus, particularly rigidity of the neck, Kernig's sign, and hyperesthesia of the skin.

INFANTILE TYPHOID

The typhoid of infancy often escapes diagnosis in spite of the fact that it gives a more or less characteristic picture. The course is often very short, and the temperature is moderate and does not show the classic curve characteristic of the disease. When diarrhea, vomiting and coating of the tongue are present, it is easy to suspect infectious diarrhea, in spite of the fact that the stools do not show the blood and excessive mucus characteristic of this disease. In other cases apathy and meningeal symptoms are so pronounced that meningitis is suspected. The difficulty of diagnosis is increased by the fact that rose-spots are less common, and splenic enlargement often difficult to detect.

COMPLICATIONS AND SPECIAL SYMPTOMS.—In general complications are much less frequent and severe in childhood than in adult life.

Digestive System.—Hemorrhage and perforation, the two most serious complications of typhoid fever in adults, are rare in childhood and are usually seen only in older children. It must be remembered, however, that these complications are possibilities.

At times pharyngitis, follicular tonsillitis, and ulcerative stomatitis are seen in the course of typhoid fever in children. These complications are particularly common when the mouth is not properly cared

for; exceptionally through secondary infection, there may be a supuration of the parotid gland.

The vomiting of typhoid fever is usually comparatively slight, and is seen only in the earlier stages of the disease. Occasionally, especially in neuropathic children, the vomiting is much more frequent, severe and persistent.

Otitis Media is the commonest complication of the typhoid fever of children. It is usually of a benign character.

Bronchopneumonia is seen at times, especially in young children of weak resistance. Its development is often very insidious.

The Circulation.—The circulatory system is only affected in severe and prolonged cases. A toxic myocarditis betrays itself by a shortening of the first heart sound, and by a pronounced tachycardia. Endocarditis and pericarditis are very rare. Bradycardia and irregular action of the heart are sometimes seen during convalescence, but have no serious significance.

The Kidneys.—A pronounced nephritis is extremely rare. The typhoid bacilli are eliminated in the urine and persist even in convalescence, but usually produce no symptoms. Occasionally, signs of pyelitis or cystitis are found in the urine.

The Nervous System.—In older children aphasia is seen at times. Signs of meningeal irritation are commoner in children than in adults, and in cases with rigidity, Kernig's sign, and spasm of the extremities, lumbar puncture often reveals either an increased quantity and pressure of cerebrospinal fluid, or a slight increase in the cell count.

The Skin.—At the beginning of the disease a toxic erythema is sometimes seen rather more often in children than in adults. Severe cases may show various forms of erythematous eruption later in the course of the disease. Not infrequently after subsiding of the fever, children have profuse sweating, which leads to the formation of sudamina, and often leads to a certain amount of desquamation of the trunk and extremities, which does not involve the face, hands or feet. Decubitus is much less frequent than in adults. On the other hand, furunculosis is not uncommon in children during convalescence.

The Bones.—Periostitis is seen at times in the typhoid fever of children. It usually occurs during convalescence, and sometimes not until the lapse of several months. The areas are usually small, circumscribed, and most frequently found upon the tibia. This complication is accompanied by slight if any febrile reaction, and is often overlooked. Osteomyelitis is very rare.

Relapses are just as common in the typhoid fever of children as in that of adults, and the course of a relapse usually bears a close resemblance to the original attack.

DIAGNOSIS.—The diagnosis of typhoid fever is in general rather more difficult in childhood than in adult life, on account of the less pronounced symptoms typical of early life. A positive diagnosis can be based only on laboratory methods. The advance in laboratory methods, however, should not lead us to minimize the importance of a purely clinical diagnosis, based on the symptoms exhibited by the patient when first seen. It is important, not only for treatment, but more especially for prophylaxis, that the physician should always be able to recognize the *possibility* of typhoid. As most of the laboratory tests by which the diagnosis is confirmed do not become positive until after the disease is well advanced, an early clinical diagnosis, even though not positive, is always desirable.

CLINICAL DIAGNOSIS.—The most important diagnostic feature of the early stages of typhoid fever is the *absence of any characteristic symptoms or definite physical signs*. For this reason the physician should always bear in mind the possibility of typhoid fever in *any acute febrile condition in which a careful history and physical examination do not reveal any adequate cause for the fever*. The diseases most commonly entering into the differential diagnosis of typhoid fever are not so much diseases which have definite symptoms suggesting those of typhoid, as diseases which, like typhoid, have indefinite symptoms. Careful daily examinations will often succeed in excluding these conditions one by one, leaving typhoid as the sole possibility, and this may be accomplished before positive laboratory evidence is obtained.

It should be remembered that while the general course of the fever and the symptom-complex may be suggestive of typhoid, they are not conclusive. The two most important purely clinical symptoms are the *roseola*, and the *splenic tumor*. When these actually *appear* in the course of the physician's observation of the case, the diagnosis is fairly certain. When they are present at the time of the first observation, they are strong evidence of typhoid, but less conclusive. The splenic tumor may be due to some foregoing condition, and the roseola may be due to something else.

The diseases most commonly confounded with typhoid fever, are those in which a routine physical examination is often or usually negative.

Lobar Pneumonia in children frequently shows no abnormal signs on physical examination of the lungs. The onset of typhoid may be as acute as that of pneumonia. In the early stages the only feature pointing toward lobar pneumonia is the increased rate of respiration. The diagnosis may remain in doubt until the appearance of signs of pulmonary consolidation on the one hand, or of rose spots or splenic tumor on the other hand. Laboratory methods,

however, will differentiate these two conditions at a very early stage, as the blood examination in pneumonia almost always shows a leukocytosis.

Certain forms of non-specific *intestinal infection* are seen, in which gastro-intestinal symptoms are not so prominent as in typical cases of infectious diarrhea. Such cases may be mistaken for typhoid. The diagnosis may be in doubt for several days, but the fever in these intestinal conditions is usually of brief duration.

The *pyelitis* so common in infancy and early childhood often bears a close symptomatic resemblance to typhoid fever. The differential diagnosis can be made at once by examination of the urine.

Miliary Tuberculosis, especially the form which eventually manifests itself in the symptom-complex of tuberculous meningitis, is often extremely difficult to distinguish from typhoid fever. The diagnosis may be in doubt for a considerable time, until finally settled by the appearance either of the splenic tumor and rose spots, or of definite cerebral symptoms. The results of lumbar puncture will often settle the diagnosis before the appearance of the Widal reaction.

General Septicemia, or malignant endocarditis, comes more rarely into the differential diagnosis of typhoid fever in children than in adults.

There are certain cases of *rheumatic fever*, in which arthritic symptoms are slight or absent, the process mainly involving the endocardium, which are difficult to distinguish from typhoid fever. Even when an endocardial murmur is present, the physician may be in doubt whether it does not represent a preexisting endocarditis.

There are also certain forms of *influenza*, in which the catarrhal symptoms affecting the upper respiratory tract are slight or absent, which clinically resemble typhoid fever. Such cases have been described as "abdominal grippe." They are rare, except in recognized widespread epidemics of influenza.

There are certain cases of typhoid fever in which there is so much pain and tenderness in the right iliac region, and so much vomiting, that *appendicitis* is suspected. In these cases, however, careful examination will usually show that involuntary spasm is absent. On the other hand, there are cases of appendicitis in which fever is prominent, and local pain and tenderness slight. The white blood count is of the first importance in the differential diagnosis of these diseases, as appendicitis practically always shows a leukocytosis.

In some cases of typhoid fever in children the signs of toxic irritation of the meninges are so prominent as to suggest some form of purulent *meningitis*. In such cases, lumbar puncture should be performed, in order to settle the diagnosis.

LABORATORY DIAGNOSIS.—There are a number of laboratory tests, which are essential to the diagnosis of typhoid fever. Some of these

require a technique too complicated for ordinary clinical use, their place being in the research laboratory.

For ordinary use, there are three tests which can be made with comparatively simple technique. These are:

1. The Widal Reaction
2. The White Blood Count
3. Blood Culture.

The first two of these tests should be made as a routine in every case of possible typhoid. The third test requires somewhat more of technical skill in bacteriology, but I believe should be much more widely used in the diagnosis of typhoid fever.

The Widal Reaction.—The technique of this test has been described in Division II. A positive agglutination test rarely appears until the beginning of the second week, and may not appear until considerably later. In general a positive reaction is apt to be somewhat longer delayed in children than in adults. On the other hand, the normal child's blood has less agglutinating power than the adult's blood, so that a positive reaction with less dilution in a child points toward typhoid. Repeated tests should be made, as long as the reaction remains negative.

The Widal reaction, when positive, is diagnostic of typhoid fever, unless the child has previously had the disease or has been artificially immunized.

The White Blood Count.—The leukopenia characteristic of typhoid fever appears early in the course of the disease. Even in the earliest stage, there will be an absence of any leukocytosis. The low white blood count is less positively diagnostic of typhoid fever than the Widal reaction, but its appearance early in the course of the disease affords useful evidence in differential diagnosis.

Blood Cultures.—The taking of a culture from the blood usually involves entering a vein, and is rather a formidable operation for ordinary clinical use. It has been demonstrated, however, that the typhoid bacillus can be obtained in cultures from blood drawn from the lobe of the ear. In infants the blood can be drawn from the longitudinal sinus.

The ear is washed with soap and water, and with 70 per cent alcohol, and a deep puncture is made with a sterile scalpel. The blood is drawn into sterile pipettes, drawn to a capillary point, 1 c.c. being required. This is planted on a sterilized medium consisting of fresh ox bile, inspissated ox bile, or bile salts. The medium is incubated, and transfers to bouillon are made after six, twelve, twenty-four and thirty-six hours' incubation. The typhoid bacillus is easily recognized by its morphology and motility.

This test, like the Widal reaction, affords positive proof of the

existence of typhoid fever. It has the advantage of being positive much earlier in the course of the disease. Some writers state that by means of blood cultures a positive diagnosis can be made in the first week in from 90 to 100 per cent of cases.

Other laboratory tests will be considered under Problems and Research.

PROGNOSIS.—The prognosis of typhoid fever in childhood is good. Statistics show that the disease is much less fatal in children than in adults, and that the mortality increases directly with the age. The complications whether arising from local disturbance of the intestine or from cardiac and pulmonary disease, are rare in comparison with those encountered in later life. The disease, however, varies very much in its severity in different epidemics and in different stages, and a child may have a severe type of typhoid fever and die from it.

PROPHYLAXIS.—The various measures of isolation and disinfection required in preventing the spread of typhoid fever will not be described in detail. They differ in no way from those used in the typhoid fever of adults, and as the disease is particularly one of adult life, it will be assumed that the reader is already familiar with its prophylaxis.

ANTITYPHOID VACCINATION.—Within the last decade, inoculation against typhoid fever has been widely employed, especially among soldiers and sailors, but also to some extent in civil life. There is no doubt of the preventive power of antityphoid vaccination. Many points remain to be settled, among them being the duration of the immunity produced in this way, and the comparative value of vaccines prepared in various ways.

The vaccine most commonly employed is a suspension of heat-killed typhoid bacilli. It has been shown that severe reactions are rare, and that when small amounts of a vaccine of low virulence are used, there is little inconvenience.

There are various methods of using the vaccine. The one most often used in Boston is to give four inoculations at five-day intervals, the doses being 100 million, 200 million, 400 million, and 600 million for adults. Proportionally smaller doses are used for children. The inoculation is made in the interscapular region.

To what extent is inoculation against typhoid fever indicated in children? In considering this question, the comparatively mild character of the disease in early life has considerable weight. I have recommended antityphoid vaccination in very few cases, and then only under exceptional circumstances. I believe that the vaccination of children should only be recommended under the following conditions:

1. If the child is to travel in parts of the world where typhoid fever is prevalent and sanitation poor.
2. If there is a pronounced epidemic of typhoid fever, the cause of which has not been found.

TREATMENT.—Typhoid fever has no specific treatment of which the value has been demonstrated sufficiently to warrant its routine use. The low mortality of the disease in childhood is a feature which would lead any method of treatment to give a false impression of effectiveness. In my opinion the secret of success in the treatment of the typhoid fever of early life is to avoid all active treatment as much as possible.

GENERAL MEASURES.—The typhoid patient, or the patient in whom typhoid is suspected, should be put to bed and kept there as long as any fever persists, and for at least a few days thereafter, no matter how mild the case. The length of time during which the patient shall be kept in bed after the temperature reaches normal depends on the severity of the case, and the strength of the patient. The precautions of isolation, disinfection of urine, feces, utensils and linen, and all the measures used in preventing the spread of the disease, should be instituted as soon as the possibility of typhoid fever is suspected, and should be continued until either typhoid is excluded as a possibility, or the patient is wholly well. When the temperature begins to fall, *hexamethylenamin* should be given in doses of three to five grains three times a day, and continued for a week or ten days after defervescence. The object of this is to remove typhoid bacilli from the urine.

The most careful nursing should be employed throughout the disease. The skin should be carefully attended to, daily sponge baths being used, and the exposed parts should be frequently bathed with alcohol. The mouth should receive careful attention, mouth-washes, syringing, or spraying being used frequently.

THE DIET.—The old idea that typhoid patients should receive a diet consisting wholly of milk, or even wholly of liquids, has been shown to be entirely wrong. An exclusive milk diet tends to produce tympanites. It has been shown that a diet rich in calories is the best for children with typhoid fever, and that with a high caloric diet the patients lose little or no weight, and may even gain. The liberal diet furthermore does not produce unfavorable results, but adds to the comfort of the patient, and appears to cause the disease to run a milder course.

The diet, however, must not be made so liberal as to produce any disturbance of digestion. The intestinal lesions of typhoid fever in childhood are comparatively unimportant, and the disease appears to produce less lowering of digestive power than most acute infec-

tions. Nevertheless the physician should always watch for evidences of indigestion from overfeeding, as shown by vomiting or undigested stools. It is also best to avoid articles of food which leave a large undigested residue, such as fruit and vegetables.

The diet should be about what a child of the same age would take in health, with the exception of fruit and vegetables. This for older children would include milk, cereals, bread or toast, beef-juice, broths, eggs, butter, minced chicken and ice cream. If the digestion of the child is normal the caloric value of the food can be further increased by the addition of some dextrin-maltose preparation, cream, or cocoa, to the milk. If there are any signs of indigestion, the diet must be reduced according to the indications. Feedings should be given at three-hour intervals by day, and one feeding at night. It is usually difficult to overfeed children with typhoid, the difficulty lying in getting them to take enough. Considerable urging may be necessary, but any form of forced feeding should not be employed except in exceptional cases.

THE BOWELS.—Constipation is best combatted by enemata, which may be ordered to be given every other day if the bowels do not move. If with this routine the constipation is accompanied by any tympanites, the enemata should be given daily.

Diarrhea requires no treatment unless the number of movements in twenty-four hours exceeds five. Bismuth should be tried first, and if this fails, opium in doses appropriate to the age of the patient should be used.

In childhood tympanites is rarely severe enough to require treatment. When marked, it may be relieved by turpentine stupes, or by the rectal tube. Glycerin suppositories and glycerin enemata should be avoided.

HYDROTHERAPY.—This method of treatment is used in typhoid fever for the control of high temperature, and for the relief of such nervous symptoms as restlessness, sleeplessness, or headache. It has not been shown to have any influence on the course or mortality of the disease. Most writers state that hydrotherapy is indicated whenever the temperature reaches a certain point. I do not entirely agree with this statement. High temperature is usually accompanied by restlessness or some nervous symptoms, and in such cases I believe that hydrotherapy is indicated. I do not believe it to be indicated just because the temperature reaches a certain point, when there are no signs whatever of any disturbance from the fever. It must be remembered that children in general do not bear cold baths as well as adults. One must be guided by the effect of hydrotherapy on the nervous system, and on the general condition of the patient, rather than by its effect upon the temperature.

Sponging with equal parts of water and alcohol at a temperature of from 85° to 95° F. is often all that is required. If this fails to relieve the symptoms, the bath should be used, the child being placed in water at a temperature of 100° F., and the temperature of the bath being lowered by the addition of colder water. The temperature of the bath should not be brought below 85° F., and the child should be vigorously rubbed while in the bath. In some cases the cold pack works better than the bath.

When hydrotherapy fails to relieve nervous symptoms, bromide of sodium may be given. Antipyretic drugs should be avoided.

Stimulation is not often required in the typhoid fever of early life. The indications and treatment are the same as in other acute infections.

Intestinal hemorrhage is treated as in adults, with absolute quiet, morphin hypodermically, withholding food by mouth, ice to the abdomen, and if necessary, normal salt solution subcutaneously. Perforation requires early diagnosis and early laparotomy.

VACCINE THERAPY.—While the prophylactic value of antityphoid inoculation is established, its therapeutic value is still an open question. In a recent review of reports on vaccine therapy in typhoid fever including 3,000 cases, I note that out of thirty-nine observers thirty-five thought they saw a favorable effect. The type of vaccine used, and the dosage and method of administration had little apparent influence.

It must be remembered that all such reports are based on clinical observation, the value of which in judging the effect of any therapeutic measure is always doubtful. The history of medicine is full of faulty conclusions based on such reports. One cannot, however, deny the possible value of vaccine therapy in typhoid fever. It must be regarded as still in an experimental stage, and we must look to the future to determine its final value.

In the meantime we are confronted by the question whether vaccine treatment is ever indicated in the typhoid fever of children. In view of the mildness of the disease in early life, I believe that it is not indicated as a routine, nor in the usual run of cases. Its value must first be proved in adults. In children, I would only advise vaccine therapy in exceptionally severe cases, but this conclusion may be changed by the work of the next few years.

PROBLEMS AND RESEARCH.—Research in typhoid fever is being devoted to the following subjects:

1. The value of antityphoid inoculation in treatment, and the best form of vaccine and method of employment in prophylaxis.
2. The nature of the immune reaction.

3. Perfecting laboratory methods of diagnosis, especially those based on biological reactions.

4. Problems in transmission and disinfection.

In vaccine therapy and prophylaxis, the principal question now under discussion is the comparative value of heat-killed vaccines, autogenous living vaccines, and "sensitized vaccines" prepared by subjecting living cultures to the action of immune serum. The use of sensitized vaccines was suggested by Metchnikoff and Besredka. It is interesting to note that in the course of their experiments, they produced typhoid lesions in a chimpanzee with fecal material from a typhoid patient, recovering the organism from the blood. There has always been a weak spot in the proof that the bacillus of Eberth was the cause of typhoid fever, as the disease could not be adequately reproduced in animals from cultures, and there was a possibility that typhoid fever was due to some undiscovered filterable virus, the bacillus being a secondary invader. Filtered fecal material failed to produce the disease in the chimpanzee, and Metchnikoff and Besredka's work gave the final fulfilment of Koch's laws. Their belief in the superior efficacy of sensitized vaccine was based on the fact that bacilli from a carrier were not virulent for this chimpanzee, but protected him from virulent bacilli, whereas vaccines made of killed bacilli did not protect him. Other observers are working with sensitized vaccines, and the most recent experimental work tends to show that the serum of persons so treated does not deviate complement, nor give an agglutination reaction, but appears to increase phagocytosis, and probably contains anti-endotoxins. It further suggests that the detecting of various specific bodies is no measure of actual immunity.

The complexity of the problem of the nature of the immunity is suggested by this work. It is evident that in typhoid fever immune bodies are many and various, and we know little of their relative importance. The finding by Gay and Claypole of a specific hyperleukocytosis on reinoculation of animals already immunized by heat-killed bacilli, is interesting in connection with the question of the nature of immunity and the value of sensitized vaccines.

There are a number of laboratory methods recently perfected, which are mainly used in the research laboratory. The technique of the isolation of the bacilli from the feces is still too complicated for ordinary clinical use, but has proved of value in the detection of carriers. It has been shown that all patients sooner or later give a positive complement fixation test, but there appears to be no relation between this and other tests based on immune reactions, and it has no value in early clinical diagnosis.

Several investigators have also found a cutaneous reaction, which they believe to be constantly present during convalescence. They

believe this reaction to be a better measure of immunity than the agglutination test, and that it may have a useful bearing on the question of revaccination in prophylaxis, and as a measure of the efficacy of various methods of producing artificial immunity. Other observers have obtained many negative reactions, and are doubtful of the value of the test.

In connection with transmission, it has been positively shown that the fly can carry the infection. Various reports tend to show that carriers are best disinfected by the use of autogenous living vaccines.

PARATYPHOID.—It is known that there is a disease bearing a close clinical resemblance to typhoid fever, but in which the blood at no time gives a positive agglutination with the bacillus of Eberth. In such cases bacilli have been isolated from the blood which bear a close resemblance to the typhoid bacillus, but which produce specific agglutinins. These have been named the paratyphoid bacillus, and two types, named A and B, have been studied. Not enough cases have been studied to enable us to say that paratyphoid infection has any constant clinical manifestations differing from typhoid.

Such cases are rare in children, but have been reported. Paratyphoid is suspected in a case which shows the clinical picture of typhoid fever, but in which the Widal reaction is constantly negative. Its existence can only be proven by testing the agglutination reactions between the patient's blood, and cultures of paratyphoid A and B, or by isolating the organism from the blood of the patient and studying its biological reactions.

The treatment is that of typhoid fever.

MALARIA

Malaria is an infectious disease, caused by the invasion of the blood with a parasite belonging to the family *plasmodidae* of the *protozoa*. Like typhoid fever, malaria is not especially a disease of early life, but occurs at all ages.

ETIOLOGY. THE PARASITE.—The plasmodia of malaria lead their vegetative existence upon red blood-corpuscles. There are at least three varieties of the malarial parasites, the *tertian*, the *quartan*, and the *estivo-autumnal*. For the detailed description of the life history of the malarial parasites, and of the appearance of the various varieties in different stages of development, the reader is referred to the general text-books.¹

The essential points to remember are the following: The malarial parasites have two cycles of development, one being that of *asexual*

¹ An excellent description will be found in *Monographic Medicine*, Vol. II, by Lewellys F. Barker, published by D. Appleton and Company, 1916.

propagation, which is carried on in the blood of the intermediate host (man), the other being that of *sexual propagation* which is carried on in the gastro-intestinal canal of the definitive host (mosquito). The early stages of the sexual forms, however, are also developed in the human blood, and it is these forms which when withdrawn by the mosquito carry on the sexual cycle. The paroxysms characteristic of the disease are produced by the *segmentation* of the mature asexual forms, which occurs at regular intervals, and which is a part of the asexual cycle. The sexual forms are resistant, latent and inactive in the blood for a long time without producing symptoms. It has further been shown that the female sexual forms are capable of undergoing segmentation without fertilization, and the small bodies thus produced may start a new asexual cycle. This accounts for latent infections and the *relapses* which are apt to occur in the spring of the year, or upon removal of a patient from one climate to another.

The asexual cycle of the tertian parasite, ending in segmentation, is repeated every forty-eight hours. The asexual cycle of the quartan parasites is seventy-two hours in length. The estivo-autumnal is the form known as tropical or pernicious malaria. The asexual cycle like that of the tertian is forty-eight hours in length.

The *tertian parasite* first appears in the red blood-corpuscles as a small hyaline body with ameboid movements. It increases in size and develops fine, dark, pigment granules, which are in constant motion, due to the ameboid contractions of the protoplasm of the individual parasites. The red cells which contain them become slightly enlarged and gradually decolorized. Each parasite when fully grown nearly fills the red corpuscle. In the stage of segmentation, which occurs at the time of the paroxysm, fifteen or twenty segments appear, which invade fresh red corpuscles, and begin the cycle again as hyaline bodies.

The *quartan parasite* resembles the tertian, but its ameboid movements are slower, the pigment granules are coarser, darker, and less active, the full-grown organism is smaller, and the red cell in which the organism develops becomes somewhat shrunk about the parasite, and of a deeper, old-brass color. It segments into only five or ten parts.

The *estivo-autumnal parasite* is smaller than the others and contains less pigment. The corpuscles containing them become shrunk and brass-colored. About a month after the onset of the attack, characteristic crescentic or ovoid bodies appear, which have coarse pigment granules clumped in the center. These are the sexual forms.

The tertian form is the one which is by far the most common in this part of the country, and the one which is most influenced by the administration of quinin; the other form, represented by the quartan,

being peculiarly difficult to manage with quinin. In young infants the tertian form in its quotidian variety is met with most commonly. In older children, in my experience, it is pure tertian that is most common. It will be noticed, on examining table 46 on page 614, that the quartan form of malaria can never represent by its intervals and paroxysms the pure tertian form.

TRANSMISSION AND EPIDEMIOLOGY.—Malaria is transmitted only by mosquitoes of the genus *anopheles*. Malaria cannot appear in a new locality without being introduced by an infected human being or by an infected mosquito. Human beings with latent infections carry the parasites through the winter, and develop an attack of malaria in the spring from parthenogenetic reproduction of the female sexual parasite. Such patients are bitten by an *anopheles* mosquito, in which the sexual cycle is carried on, the young parasites reach the salivary glands in the neck of the mosquito, and the bite of the insect infects a new human being. The parasites enter the red blood-corpuscles, and begin asexual propagation.

The ordinary house mosquitoes, which we see in most of our cities and towns, excepting in the very malarious districts, do not belong to the harmful class. They belong to the genus *culex*. The main differences between the *culex* and the *anopheles* are readily made out. In the first place, all the common forms of *culex* which we see have wings free from marking, beyond the ordinary veins. All three varieties of *anopheles* positively known in this country have spotted wings. The most important and simple distinction, however, is the manner in which these varieties of mosquitoes sit on the wall. The *culex* sits on the wall with its body parallel to the surface to which it is attached and the posterior pair of legs raised over its back. The *anopheles*, on the other hand, sits with its body sticking out from the wall at an angle of forty-five degrees or greater, with the posterior pair of legs, which are very long, resting against the wall or hanging down. When such a mosquito is sitting on the ceiling he looks often as if he were hanging from his proboscis. This distinction is readily made out by any layman. The *anopheles* and *culex* are represented in Plate XV opposite page 120. A third point is the difference of the mouth parts. The ordinary house mosquito, the *culex*, has a single proboscis, at the root of which are two little, short, stump-like processes, the palpi. In the *anopheles* these palpi are of a length almost equal to the proboscis, so that on superficial examination the mosquito looks as if he had three proboscides.

The *anopheles* multiplies in stagnant water. It does not multiply in running water, nor in large bodies of water. Malaria does not occur in latitudes farther north than 60° nor farther south than 40°. Where there is no *anopheles* there can be no malaria (except imported cases).

PREDISPOSITION.—It is probable that every human being bitten by an infected anopheles, will develop the disease. In malarial regions the disease is very common in infants and young children, at least as common if not more common than in adults. This is probably because young children are so frequently bitten by mosquitoes.

PATHOLOGICAL ANATOMY.—There are no especial differences between the pathological lesions found in the malaria of children and those which occur in adults. According to Thayer, in *acute* cases of malarial fever, on examination with the microscope, the cerebral capillaries are found to be crowded with malarial parasites. There is usually a marked granular degeneration of the endothelium of the vessels.

The *spleen* is always enlarged, often only moderately. The parenchyma is cyanotic, of a slaty-gray color, and almost diffuent. The pulp of the spleen is found to contain enormous numbers of red blood-corpuscles, many of which contain parasites. Great numbers of white cells are also seen, some of them being necrotic. The capillaries are usually filled with red blood-corpuscles containing the plasmodia, while the splenic veins show relatively few, although they always contain large cells enclosing pigment or the remains of red blood-corpuscles.

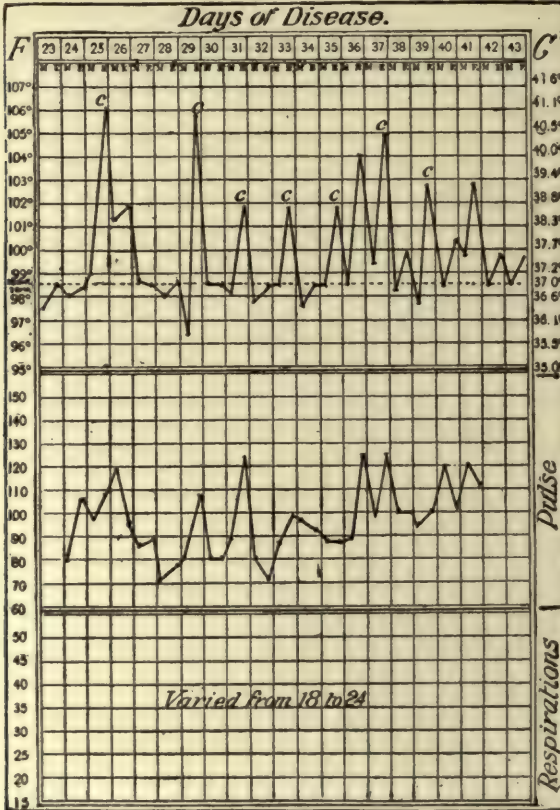
The *liver* is swollen and has usually a slaty-gray color. The capillaries are filled with leucocytes, which contain numerous pigmented bodies. Relatively few plasmodia are found in the blood-corpuscles in the vessels. Areas of disseminated necrosis similar to those in other acute infectious diseases have been described.

The vessels of the *kidneys* contain relatively few organisms. The glomeruli may be considerably pigmented. There may be marked degeneration of the epithelium of the capsule, and at times changes in the parenchyma, especially areas of necrosis of the epithelium of the convoluted tubules. The other viscera show no special characteristic changes, except, at times, that of melanosis.

SYMPTOMS.—The symptoms of malaria as the disease occurs in infants and young children are much more varied and far more uncertain than those which we are accustomed to meet with in adults. The prominent symptom of malaria being the paroxysm, earlier authors naturally classified malaria according to the time when the paroxysms appeared, using the term quotidian when they occurred with intervals of twenty-four hours, tertian when they occurred with intervals of forty-eight hours, and quartan where they occurred with intervals of seventy-two hours. Again, the terms *intermittent* and *remittent* have been used commonly. The intermittent form is characterized by entire absence of fever between the paroxysms. The

remittent form is characterized by the presence of more or less fever of a continued type which does not cease between the paroxysms. These terms should not be used as classifications of distinct types of malaria, as the conditions which they represent may, according to chance, appear in any of the types, and are merely caused by a variation in the behavior of the parasite. In tertian and quartan malaria in adults the parasites all tend to reach the segmenting stage

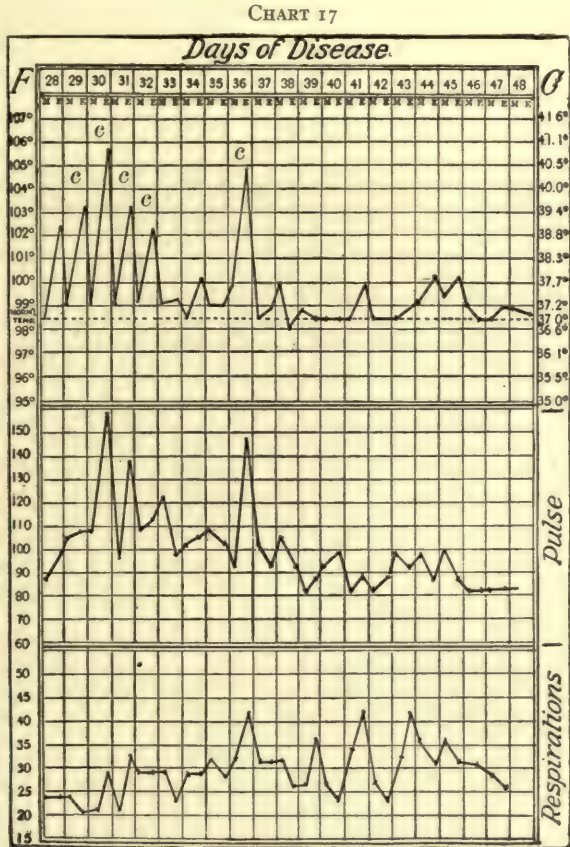
CHART 16



Pure tertian form of malaria. (C means chill.)

at about the same time, so that with a single group or generation of parasites the paroxysms will occur at regular intervals of two days for the tertian, and three days for the quartan. There may however be more than one group or generation of parasites in the blood of the patient. If more than one generation of parasites exists in the blood in a tertian case, the fever may become quotidian, with daily paroxysms due to the ripening of distinct sets of parasites on different days, each set of parasites taking forty-eight hours to mature.

In like manner, in cases of quartan fever, through the ripening of distinct sets of parasites on different days, different combinations occur, according to the number of sets of parasites. Thus, while in the form in which there is only one generation the intervals between the paroxysms are seventy-two hours, in that in which there



Double tertian form of malaria (quotidian). (C means chills.)

are two generations there may be an interval between the paroxysms of only forty-eight hours, and when there are three generations there may be an interval of only twenty-four hours, thus representing the quotidian chills described by Mannaberg. The following table explains the different types of paludism as they are now understood by the most recent investigators:

TABLE 53

The Principal Combinations of Paroxysms Caused by the Plasmodium Malariae

	INTERVALS	1ST DAY	2D DAY	3D DAY	4TH DAY
TERTIAN					
Pure tertian (One parasite)	48 hours	Paroxysm	No paroxysm	Paroxysm	No paroxysm
Double tertian (Two parasites. Quotidian)	24 hours	Paroxysm	Paroxysm	Paroxysm	Paroxysm
QUARTAN					
Pure quartan (One parasite)	72 hours	Paroxysm	No paroxysm	No paroxysm	Paroxysm
Double quartan (Two parasites)	48 hours	Paroxysm	Paroxysm	No paroxysm	Paroxysm
Triple quartan (Three parasites. Quotidian)	24 hours	Paroxysm	Paroxysm	Paroxysm	Paroxysm

The table explains how the different intervals in the paroxysms are caused by the development of the parasite on different days. It will therefore be understood that it is according as the parasite happens to develop that we have a regular or an irregular periodicity. Thus, it may happen that we have two parasites, and these two parasites may develop on the same day, but at different hours. In this case, supposing that they are of the tertian type, two paroxysms may occur on the same day, followed by an interval of forty-eight hours from the time of the full development of each of the parasites until this development occurs again. In this way different broods of parasites may cause an almost infinite variety of symptoms. In estivo-autumnal fever there are numerous generations, so that the symptoms have no definite periodicity.

In general, in children there is a tendency in all types of malaria towards a deviation from the regular arrangement of parasites in groups, so that even in tertian and quartan fever the regularity of the manifestations appears to be not so striking as in adults.

The onset is usually acute with vomiting and prostration. The temperature is high, ranging from 104° to 106° F. The respiration is often feeble or harsh over the back of one or both lungs, sometimes with coarse moist râles, and usually a slight increase of vocal fremitus and slight dulness on percussion. These signs and symptoms may disappear in the course of a few hours with the fall in temperature, and may recur on the following days until quinin is administered.

The younger the individual the more likely are the pronounced *chills* to be replaced by some other symptom, such as vomiting, delirium, or convulsions. The paroxysms are often less distinctly marked, and appear to come more frequently in children than in adults, and in young children a condition of apathy and somnolence,

sometimes with fever, and sometimes accompanied by coldness of the extremities and a collapsed condition very commonly replaces the chill of the adult. These symptoms, representing the onset of the disease, may often disappear as the disease becomes established, and in their place we may meet with the symptoms of some other disease. The susceptibility of the nervous and respiratory systems in young children tends to produce variations in the form and type of malaria which are misleading in regard to diagnosis, the symptoms referable to a particular organ often completely overshadowing the real disease, malaria, and producing an entirely new clinical picture. The symptoms often are so indefinite, and the disease frequently comes on so insidiously, that the physician does not see the case until it has made considerable progress and the diagnosis is thus much obscured.

FIG. 143



Boy, 9 years old. Enlarged spleen. *Plasmodium malariae* found in the blood

In addition to the other symptoms, severe pain in the head and sometimes in the epigastric region is met with. In the form in which the invasion is gradual, the prominent symptoms are anemia, loss of appetite, and frontal headache of moderate type. Splenic or hepatic tenderness, pains in the back, extremities, and neck, and general cutaneous hyperesthesia are occasionally observed.

PHYSICAL EXAMINATION.—The only constant physical sign in malaria is enlargement of the spleen. This occurs rather more rapidly in children than in adults, although there is considerable variation in the date when the splenic tumor can first be detected.

COMPLICATIONS.—Bronchitis has been found to be the most frequent of all the complications occurring in the course of malaria in children, and again and again has proved to be intractable until its malarial origin was discovered. Certain acute cases appeared to be dependent upon pulmonary congestions analogous in their pathology to the congestions of the spleen and the liver. Pneumonia, both lobar and lobular, has occasionally been found as a complication of malaria. Spasmodic asthma of malarial origin has been seen in some cases. These attacks were accompanied frequently by marked splenic enlargement, and were promptly relieved by quinin.

FIG. 144



Girl, 9 years old. Enlarged spleen. *Plasmodium malariae* found in the blood

The condition of the intestinal tract varies as much as do the other symptoms. Sometimes constipation is present and sometimes diarrhea, the latter being the more prominent the younger the child.

Subacute and *chronic* forms of malaria occur in children as in adults, characterized by anemia, splenic enlargement, a low grade of fever, and the presence of the parasites in the blood.

DIAGNOSIS.—Malaria as it occurs in early life is far more difficult to diagnose by its symptoms than when the disease runs the typical course usually seen in the adult. It is the most protean disease which we are called upon to deal with in young children, and it simulates so closely so many other conditions we are likely to meet with that we should always be on our guard, and allow for the possibility of the presence of the plasmodium malariae in making a diagnosis in any doubtful case. Whenever there is any periodicity in the symptoms, or whenever there is definite splenic enlargement, malaria should be suspected. The only rational method of determining whether we are dealing with a case of malaria is by an examination of the blood, which at once settles the question if the plasmodium is discovered. The parasite can usually be found in a patient who has had little or no quinin, if the blood is thoroughly examined during a paroxysm by a person who has had considerable experience. Both the fresh and the stained specimens should be examined. The absence of leukocytosis in malaria is an important aid in the exclusion of chills and fever dependent upon septic processes.

PROGNOSIS.—The prognosis of malaria in children is good, provided that the child is removed from the malarial district and is treated with quinin. Relapses occur, even after long intervals of apparent immunity, and the disease can recur a number of times.

PROPHYLAXIS.—The value of mosquito-nets from a prophylactic standpoint is significant, and observations in malarious districts during the last year or two strongly support this idea. The fact that a patient with malarial fever in a malarious district is a source of danger to those about him is a very important one, the deduction being, of course, that one should insist upon such an individual sleeping under a mosquito-net. The importance also of early and thorough treatment of all cases of malaria, particularly relapses in the early malarial season, is evident. In some regions destruction of the mosquito larvae has accomplished a great deal.

TREATMENT.—Malaria is one of the few acute infectious diseases for which there is a specific drug treatment. *Quinin*, when properly given, will bring about a rapid cure in all cases caused by the tertian parasite, and in most cases caused by the other varieties.

METHODS OF ADMINISTERING QUININ.—Quinin may be given by mouth, by rectum, subcutaneously, or intravenously. As a routine, in the majority of cases the drug should be given *by mouth*. Infants do not usually object to the taste, but they cannot swallow an insoluble form of quinin. It is therefore best in infants to use the *bisulphate* in aqueous solution. A convenient preparation is to make this up to contain two grains to the teaspoonful. If this solution is

vomited or not taken well, a similar solution may be given by rectum, in double the dose and diluted with three ounces of water; or the bisulphate may be given in a rectal suppository. It is sometimes advisable to give part of the dose by mouth, and part by rectum.

For children old enough to object strongly to the taste of quinin, but still too young to swallow capsules, the aqueous solution of the bisulphate may be combined with syrup of sarsaparilla, orange or yerba santa. Rectal suppositories may also be used at this age. For still older children the sulphate may be given in gelatin capsules.

The hypodermic and intravenous routes are only to be used when for some reason the above methods fail, or in very exceptionally severe cases. The preparations adapted to subcutaneous administration are the bimuriate of quinin and urea, the hydrobromate, and the bisulphate. All are irritating, and the injection is sometimes followed by sloughing. It is better if possible to avoid subcutaneous injections, and they are rarely indicated in early life. In infants with an open fontanelle, a solution of the bisulphate diluted in an ounce of water may be easily given into the longitudinal sinus, but this is only indicated in very severe cases.

DOSAGE.—I believe that the most important requisite in the treatment of malaria with quinin is to administer the drug in such a way that the maximum quantity is circulating in the blood at the time of the paroxysm, or, if there be no definite paroxysm, at the time of the maximum intensity of the symptoms. For this purpose, if the case is not exceptionally severe, it is best to wait for two or three days before beginning treatment, keeping the patient under close observation, with a four-hourly temperature record. This will show the periodicity of the paroxysm, or of the maximum temperature. I am accustomed to administer the quinin only on days when a paroxysm is expected, and to give the whole twenty-four hour amount in three doses, at two-hour intervals, timed so that the last dose will be given four hours before the paroxysm is due. The following table shows the dosage and times of administration of the bisulphate of quinin for children of various ages, under the supposition that the paroxysm will occur at 6 P. M.

TABLE 54

Dosage of Quinin in Malaria, Paroxysm at 6 P. M.

AGE OF CHILD	10 A. M.	12 M.	2 P. M.
1st year	gr. IV	gr. II	gr. II
1- 2 years	gr. VI	gr. III	gr. III
2- 5 years	gr. VIII	gr. IV	gr. IV
5-10 years	gr. X	gr. V	gr. V

If the paroxysm occurs at some other time, the doses can be arranged in the same way so that the last dose will be given four hours

before the paroxysm is due. The doses have to be rather large. Children bear quinin well, and the mistake usually made is to give too little. The large dose is given first, in order that if the child has any idiosyncrasy toward quinin, symptoms of disturbance will appear in time, and the second and third doses may be omitted.

Except for the three doses before an expected paroxysm, no other quinin is given. Used in this way the quinin should entirely abort the paroxysm. Each generation of plasmodia is attacked in this way *twice*. For example, in a single tertian infection, the quinin should be repeated once on the day when the next paroxysm would naturally occur. In a double tertian infection, the quinin should be repeated daily for three days, four days in all. If however the quinin does not entirely prevent the first paroxysm, that generation of parasites should be attacked a third time, the rule being to attack each generation once more after the paroxysm has been prevented.

After the paroxysms have been attacked as described above, I do not consider it wise to continue to give quinin in smaller doses "to make sure," as is usually done. If any parasites have escaped the original onslaught, they will not be destroyed by the smaller doses given "to make sure," but will only be prevented from developing and causing fresh symptoms. They may thus remain latent in the blood, and may cause a relapse at some distant future time. I believe the practice of continuing quinin in small doses is responsible for many incomplete cures and subsequent relapses. My practice is to *give no more quinin* as long as I can keep the patient under close observation, with a four-hourly temperature record. This permits an opportunity for undestroyed parasites to develop and to cause symptoms, in which case the original treatment is repeated. Before the final discharge of the case, the blood is carefully examined as a further precaution. Sometimes when the case is about to be released from close observation, I give more quinin to make sure, but under such circumstances I give the full twenty-four hour amount used in the original attack, in three doses at eight-hour intervals, for two or three days.

If the clinical picture is very indefinite with no recognizable paroxysms nor periodic times when the symptoms show a maximum intensity, the same quantity of quinin should be given each twenty-four hours as in the table, but the doses must be differently arranged, and the twenty-four hour amount should be divided into three nearly equal portions, which are given three times a day. This should be continued for two days after all symptoms have disappeared, and then all quinin should be omitted until symptoms reappear, or till the patient is discharged.

Malaria rarely requires any symptomatic treatment, because although there are many functional disturbances and subjective

symptoms seen in the disease, they are rapidly relieved by the specific treatment. Occasionally an infant is so much collapsed at the time of the first paroxysm that it requires stimulation. The hot pack is excellent in such cases.

In chronic cases, iron, and sometimes arsenic are required in the treatment of the anemia which accompanies the disease.

IV. DISEASES TENDING TO OCCUR IN EPIDEMICS

This group includes two diseases which tend to occur in epidemics, but in which the essential facts about the mode of transmission are still unknown. These diseases are *epidemic cerebrospinal meningitis* and *acute polio-myelo-encephalitis*.

EPIDEMIC CEREBROSPINAL MENINGITIS

(Meningococcus Meningitis). (Cerebrospinal Fever).

The term cerebrospinal meningitis refers to an acute infection of the leptomeninges, which may be due to a variety of microorganisms. Among the bacteria which produce the lesions of acute leptomeningitis, there is one variety which produces no other disease process in the human body. This variety of meningitis may therefore be considered a *specific* form, and on account of its tendency to occur in epidemics, the term *epidemic* is used in differentiating it from other etiological varieties of cerebrospinal meningitis. These other varieties are not specific, as the organisms which produce them can also cause other disease processes; they will be described in the Division on Diseases of the Nervous System.

ETIOLOGY. THE MICROÖRGANISM.—The specific organism of epidemic meningitis is the *diplococcus intracellularis meningitidis* (Weichselbaum), or, as it is now generally designated, the *meningococcus*. The organism occurs in pairs, and closely resembles the gonococcus in its biscuit-shaped morphology. It is Gram-negative, and stains readily with methylene blue, and with other basic anilin dyes. It is found in the meningeal exudate, and, in the acute stage of the disease, is always present in the cerebrospinal fluid obtained by lumbar puncture. In recent untreated cases the cocci are both extra- and intracellular; in late or serum-treated cases they are chiefly intracellular. The coccus is sometimes difficult to grow on artificial culture media. It grows best at 37° C. on media containing human or animal serum, such as blood-agar, or ascites-agar; the best medium is ascites-agar to which some glucose has been added.

The meningococcus is extremely sensitive to injurious agencies of all kinds. It dies out quickly in cultures unless frequently transplanted, and is very sensitive to light, drying, and even to dilute saline solution. It has never been found outside the body. It is almost non-pathogenic for animals, except young mice and guinea-

pigs, but when injected into the subarachnoid space of monkeys, it causes meningitis. Horses and rabbits injected with dead cocci in increasing doses, yield a serum rich in specific agglutinin, and in other immune bodies.

TRANSMISSION.—In spite of the epidemic occurrence of the disease, the complete facts as to its transmission are unknown. In the New York epidemic of 1904-5, the meningococcus was found in the nasal secretion of 50 per cent of the cases examined in the first two weeks of the disease, and in 10 per cent of healthy persons in close contact with the cases. Furthermore, Flexner has demonstrated the presence of the organism in the nasal secretions of monkeys which had been infected by intraspinal inoculation. These observations suggest that the nasal mucosa is a channel of elimination, and probably also a portal of entry. From the analogy of other diseases having a similar portal of entry and channel of exit, one would expect epidemic meningitis to be highly contagious.

Nevertheless, the disease is not very contagious. In the New York epidemic of 1904-5, only one person in a household was infected in 75 per cent of the cases, although isolation was not employed. Both at the Children's and at the Infants' Hospitals in Boston cases of epidemic meningitis have always been treated in the open wards with other patients, yet I have never seen an instance of the disease developing in a hospital patient or attendant. The instances in which such an occurrence has been reported are so few that they could be explained on the ground of coincidence. In the sporadic cases which I have seen every year in Boston and its vicinity, I have never been able to trace the infection to a source in another meningitis patient.

It seems probable from the evidence that epidemic meningitis is spread by the intermediation of healthy *meningococcus carriers*. That such carriers exist, has been demonstrated. In an epidemic the disease is relatively most prevalent in the crowded tenements, where exposure to a carrier would be most likely to occur.

But how can such a means of transmission be reconciled with the peculiar epidemiology of the disease? In every large city epidemics occur from time to time, but at rather long intervals, averaging about ten years. After each epidemic the disease remains prevalent with gradually lessening frequency of occurrence for several years until the average incidence of the disease is reached. A certain number of sporadic cases are always seen each year. In the smaller towns and remote country districts occasional epidemics are seen occurring at much longer intervals, which last for a few months, after which the disease disappears completely.

These facts can best be explained on the ground of a variation in the virulence of the specific microorganism. It is known that patho-

genic parasites in their struggle for existence, have the faculty of acquiring from time to time new powers of attack and defence. They may take on an increased power of resistance against antagonistic influences ("fastness"), or an increased power of developing in the tissues of the host (virulence). The work of Rosenow with the streptococcus group suggests that an increase of virulence may take place in the tonsillar crypts. It is conceivable that at times a similar increase in virulence may take place in the meningococci carried in the nasopharynx of a healthy carrier. This is the best available explanation of the peculiar features of the transmission and epidemiology of epidemic cerebrospinal meningitis.

PREDISPOSITION.—On account of the unknown facts as to transmission and mode of infection, the general predisposition toward epidemic meningitis cannot be estimated. The disease is much commoner among children than among adults, although it can occur at all ages, and is not uncommon in young adults. About 50 per cent of all cases are seen in children under the age of five years, and about 10 per cent of these in infants under one year. The youngest patient I have seen was three weeks old.

Epidemics are usually seen in the winter and early spring, and most of the sporadic cases also occur at this season. In Boston the disease is most prevalent in March, April and May, and is very rarely seen in the summer and autumn.

IMMUNITY.—On account of the peculiarities of the incidence of the disease, it is not known whether an attack confers any lasting immunity.

PATHOLOGICAL ANATOMY.—The lesions produced by the diplococcus intracellularis are not specific, and show no essential differences from those produced by other organisms. They will be described under Meningitis in the section on Diseases of the Nervous System.

SYMPTOMS.—Epidemic cerebrospinal meningitis presents itself as a severe, acute, febrile disease, with a great variety of symptoms referable to the lesions of the central nervous system. These symptoms are most conveniently described in the order in which they would be noted by a physician when called to see a case of meningitis.

THE HISTORY.—In taking the history the physician should inquire particularly as to the onset, fever, headache, other subjective symptoms, vomiting, convulsions, and the mental condition of the patient.

*The Onset** is usually, though not invariably, extremely sudden. *Fever* is ordinarily sufficiently marked to have been noted by the

* In order that the reader may at once gain an idea as to the frequency of occurrence of the various symptoms and signs, those which occur in more than half the cases are printed in *italics*.

child's mother or attendant. *Headache* is probably present and severe at the onset of most cases, but infants and young children do not complain of headache, so that a definite history of this symptom can be obtained in only a little more than half the cases. In addition to the headache there may be pain in the back and extremities. *Vomiting*, usually repeated, and often projectile, with no relation to meals, is seen at the onset of a majority of the cases. The most severe vomiting is seen at the onset, but this symptom may continue to occur occasionally in the later course of the disease, or may cease after the first twenty-four to forty-eight hours. Convulsions may occur at the beginning of the disease. Holt states that they were seen at the beginning of 30 per cent of his cases. In my series they were present in only 15 per cent. They are rare occurrences after the onset. A chill is rare at the onset of meningitis in children.

The mental condition of the patient in the interval between the onset of the disease and the time when the patient is seen by the physician, is one of the most important points in the history of a case of suspected meningitis. In only the very mildest cases is it unaffected. There may be only marked apathy, but delirium is fairly common, and complete unconsciousness may develop with great rapidity early in the course of the disease.

The most typical mode of onset in epidemic meningitis is the simultaneous occurrence of vomiting and severe headache, immediately followed by high fever, marked prostration, and some clouding of the mentality.

THE PHYSICAL EXAMINATION.—Ordinarily, owing to the severity of the disease, cases of epidemic meningitis are seen comparatively early, usually within the first three days.

Fever is invariably present at this stage. In the great majority of cases the temperature is high, but it may be moderate, and rarely it is only very little elevated. The tongue is dry and coated. The *pulse* is usually much accelerated, but occasionally is notably slow. The respiration may be disturbed in rhythm, but is rarely accelerated. Cheyne-Stokes respiration is occasionally seen in severe cases. Prostration varies with the severity of the case.

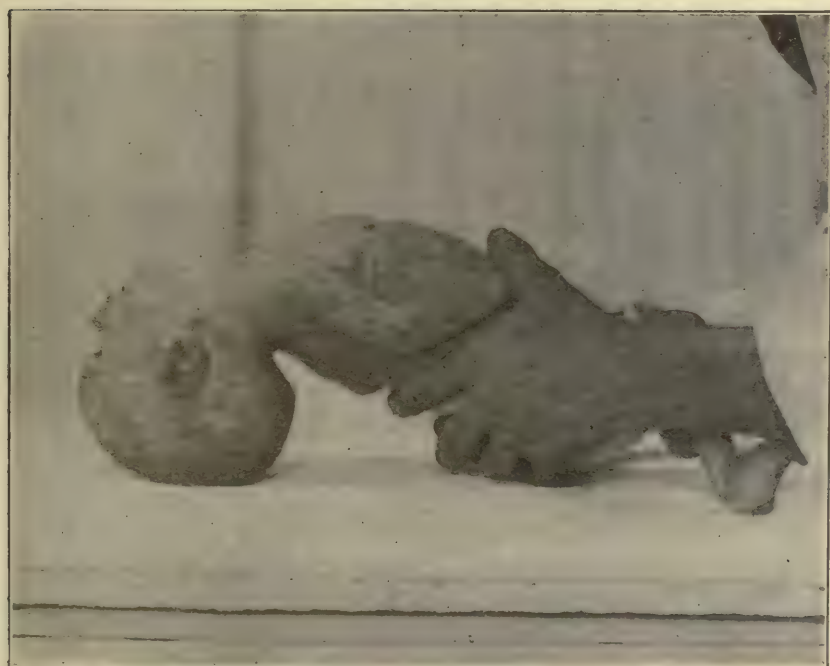
The *mental condition* is usually notably affected. In the milder cases there is only *apathy*, the children being usually very irritable when disturbed. *Delirium* is frequently present. In severe cases the patient is either comatose, or reacts very slightly to external stimuli. When unconsciousness is present, it develops comparatively early in the course of the disease. A normal mental condition, while occasionally seen, is against the diagnosis of epidemic meningitis, especially if other meningeal symptoms be at all marked.

Rigidity of the neck, while not always present when the patient is first seen, is one of the commonest physical signs in epidemic menin-

gitis. It is nearly always present at some time during the disease. In addition to rigidity, *pain on motion of the neck*, and tenderness to pressure, are often found. There is frequently marked retraction of the head, and there may be a more or less marked opisthotonos.

The *pupils* are usually contracted in the early stages of the disease, while in the later stages they are apt to be widely dilated. The pupillary reaction to light is often sluggish, and in very severe cases it may be absent. Strabismus is a rare symptom. Sometimes, especially in the later course of the disease, blindness may be detected; ophthalmoscopic examination shows it to be due to optic neuritis, retinitis, or congestion of the fundus. Photophobia is often a notable symptom.

FIG. 145



Opisthotonos in meningitis

Examination of the heart, lungs and abdomen reveals nothing abnormal beside weakening of the heart sounds, unless some complication is present.

A marked *tonic spasm of the muscles* of the extremities is a common symptom. The muscles are involved to a variable extent; at times all the limbs are very rigid. Attempts to move the limbs may cause severe pain. Muscular tremor is seen at times. Actual paralysis of a muscle or group of muscles is rare in epidemic meningitis, an im-

portant point in differential diagnosis. When paralysis is present it is either of brief temporary duration, or else it appears late in the chronic stage of the disease.

Kernig's sign is present in the great majority of cases, but is not diagnostic of meningitis, nor does its absence rule out this disease. *Brudzinski's neck sign** is usually present, but is also not diagnostic. The *knee-jerks* are, in the order of frequency, absent, exaggerated, or normal. Ankle clonus is occasionally present.

Hyperesthesia of the skin is often marked.

The frequency of efflorescence upon the skin varies in different epidemics. The most typical eruption consists in small punctate hemorrhages, which are sparsely scattered. They may appear on any part of the body, but are most often seen on the chest, neck, and

FIG. 146



Showing extreme opisthotonos in a case of chronic cerebrospinal meningitis
The hands of the attendant are only steadying the body

extremities. Sometimes the petechial spots are larger. The popular name "spotted fever" had its origin in this eruption. It was present in 20 per cent of the cases in my series. Various forms of toxic erythema of brief duration are seen in some cases. Herpes labialis is sometimes seen in older children.

The blood shows regularly a leukocytosis, averaging from 15,000 to 40,000, the increase involving the polymorphonuclear neutrophiles. The urine shows no characteristics other than those seen in any acute febrile disease.

VARIATIONS IN SEVERITY, COURSE, DURATION, AND TERMINATION.—For the purpose of estimating the prognosis and the results

* These signs are described under the physical examination of the nervous system in Division II.

of treatment, cases of epidemic meningitis may be divided into four types, as follows:

1. *The fulminating type*, in which the course of the disease is so severe and rapid that death occurs in the first twenty-four or forty-eight hours. These patients when first seen are already in an extremely serious, if not moribund, condition, with profound coma, extreme prostration, and signs of beginning circulatory failure.

2. *The severe type*, in which there is an early development of severe symptoms, but in which the course of the disease is not so rapid as in the fulminating type. There is a pause in the progress of the disease after the onset, the patients remaining in *statu quo*. When first seen such patients are either unconscious or in violent delirium, with poor general condition.

3. *The common type*, in which the patients when first seen are not unconscious, but are either very apathetic or in mild delirium, with fairly good general condition.

4. *The mild type*, in which the patients have headache, fever, and rigidity of the neck, but are perfectly rational, with good general condition.

The symptoms in epidemic meningitis are apt to reach their maximum severity early in the course of the disease.

The most common deviations from the symptoms described above are seen in infants, in whom the onset is often less sudden than in older children, and the signs pointing to irritation of the central nervous system less pronounced. It is not uncommon in infants to find present only the symptoms of fever and clouding of the mentality, the rigidity of the neck and limbs not being pronounced. In infants, however, there is the very important sign of tense prominence of the fontanelle, which is almost invariably present in all forms of meningitis.

The course of the disease has been much influenced by serum therapy. The description which will be given here applies to the course of the disease as it was observed before the days of serum treatment, and as it is now observed in cases which prove resistant to the specific treatment.

In the fulminating type death invariably occurred within twenty-four to forty-eight hours, and even with serum therapy, most cases of this most severe type die before the serum has time to produce an appreciable effect.

In the severe type of the disease, after the stormy onset, there is usually a period of variable duration in which there is not much change in the patient's condition. In the majority of cases of this type, death occurs, apparently from exhaustion, within the first three weeks. In some of these severe cases, however, the patients live longer, and after a period of about six weeks of active febrile

symptoms, enter the so-called chronic stage of the disease. In this condition the temperature is normal for a greater part of the time with occasional rises of a few days' duration, but the patients remain continuously unconscious with continued spasm of the extremities. This condition continues for an indefinite period, sometimes running into many weeks or even months. The symptoms of this chronic stage probably represent the effect of the damage done by the infectious process in the first six weeks, which damage persists after the infection itself has been stamped out. Hydrocephalus is the principal gross lesion found in such cases. In this chronic condition emaciation finally reaches an extreme grade, and death eventually occurs from exhaustion.

In the common type of the disease, at any period within about the first six weeks the symptoms may grow worse and the patient die as in the severe cases. In other cases of this grade of severity, after a period of from three to six weeks of active symptoms, the temperature comes down by a gradual lysis, the other symptoms gradually disappear; and a slow convalescence sets in, eventually leading to recovery. In still other cases of this type there is a similar fall of temperature, but the symptoms do not wholly subside. The patients then enter a chronic stage in which the symptoms are similar to those seen in the severe type, with occasional rises of temperature, persistence of rigidity of the limbs, some clouding of the mentality, and severe emaciation. In these cases recovery may eventually occur, or after a long period death may take place from exhaustion.

In the mild type of the disease the fall in temperature by lysis begins in about three weeks or even less, and a more rapid convalescence is seen.

COMPLICATIONS AND SEQUELAE.—The most common complications which occur in the course of epidemic meningitis are, otitis media, bronchopneumonia, conjunctivitis, and bed sores. Nephritis and arthritis are comparatively rare.

Permanent sequelae were more common before the use of serum therapy, and are still seen at times. The disease may leave behind various forms of paralysis, such as strabismus, facial paralysis, monoplegia, hemiplegia, or diplegia. Permanent contractures of the extremities are seen at times. Deafness, which usually involves both ears, is another serious sequela. Blindness is somewhat less common and is often unilateral. Various grades of defective mentality, which may amount to pronounced idiocy may follow an attack of epidemic meningitis. In most cases hydrocephalus complicates the chronic stage of the disease.

DIAGNOSIS.—The diagnosis of epidemic cerebrospinal meningitis depends entirely upon the results of lumbar puncture. All of

the symptoms of the disease may be either present or absent, and the diagnosis cannot depend upon any particular symptom or set of symptoms. There are a number of diseases in which symptoms of meningeal irritation are part of the clinical picture. In many of these conditions the meningeal irritation may produce not only stimulation of the cells of the central nervous system, but may even produce increase in the tension of the cerebrospinal fluid. This condition is often spoken of as *meningismus* as distinguished from true meningitis. In it there is no actual infection of the meninges, but only irritation from toxins produced elsewhere. In many cases in which this condition of meningismus is present, the clinical picture presented resembles that of epidemic meningitis in every way, and they can only be distinguished from cases of meningitis by the results of lumbar puncture.

My experience as the distributor of the Flexner serum throws an interesting light on the frequency with which other diseased conditions are mistaken for cerebrospinal meningitis. During the period in which occurred 142 cases of cerebrospinal meningitis, I was also called to administer serum in 88 cases which had been diagnosed as cerebrospinal meningitis, but which proved to be other diseased conditions, and not any form of meningitis. The diseases which thus sufficiently simulated meningitis as to lead to a demand for serum, are shown in Table 48.

TABLE 55

List of Diseases Diagnosed as Cerebrospinal Meningitis on the Basis of Their Symptom

DISEASE	CASES
Lobar pneumonia.....	29
Gastro-enteric intoxication.....	15
Anterior poliomyelitis.....	10
Otitis media.....	9
Encephalitis.....	8
Typhoid fever.....	5
Rheumatic fever.....	3
Cerebral hemorrhage.....	3
Solitary tubercle.....	2
Cerebellar tumor.....	2
Measles with pneumonia.....	1
Tetanus.....	1

Table 49 shows the frequency with which the various symptoms and signs of cerebrospinal meningitis occurred in this list of diseases.

TABLE 56

Frequency of Occurrence of Symptoms and Signs of Meningitis in List of Diseases Mistaken for Meningitis

	RIGID NECK	CLOUDED MENTALITY	UNCONSCIOUSNESS	KERNIG'S SIGN	CONVULSIONS	LOCALIZING NEUROLOGIC SIGNS	HEADACHE	VOMITING
Lobar pneumonia.....	26	29	2	22	8	1	15	23
Gastro-enteric intoxication	10	14	6	8	7	2	1	15
Anterior poliomyelitis.....	9	1	0	6	1	10	9	8
Otitis media.....	8	6	0	4	3	0	2	8
Encephalitis.....	6	8	1	7	6	8	6	8
Typhoid fever.....	5	5	0	3	1	0	5	4
Rheumatic fever.....	3	0	0	3	0	0	2	1
Cerebral hemorrhage.....	0	3	3	1	1	2	0	1
Solitary tubercle.....	0	2	2	0	2	1	2	2
Cerebellar tumor.....	0	2	0	0	2	0	2	2
Measles without pneumonia.....	1	1	0	1	1	0	1	1
Tetanus.....	1	0	0	1	1	0	0	0

It appears from Table 49 that any one of the clinical symptoms or signs considered characteristic of cerebrospinal meningitis, may appear in diseased conditions other than meningitis.

In not all the cases shown in Table 48 was it possible to make a diagnosis on clinical grounds. In thirty-seven of these cases, by the time I had reached the bedside of the patient, the case had sufficiently developed to allow a positive recognition of the actual disease present, and cerebrospinal meningitis was excluded, and no lumbar puncture was performed. There remained, however, fifty-one cases in which cerebrospinal meningitis could not be excluded, and in which it was deemed advisable not to deprive the patient of the benefit of the Flexner serum unless epidemic meningitis could first be excluded. In these cases, shown in Table 50, lumbar puncture was performed, the result excluding meningitis, and the true diagnosis appeared later in the course of the disease.

TABLE 57

Diseases Seen During a Series of 142 Cases of Cerebrospinal Meningitis, in Which Meningitis Could be Excluded Only by Lumbar Puncture

DISEASES	CASES
Lobar pneumonia.....	13
Gastro-enteric intoxication.....	12
Otitis media.....	8
Encephalitis.....	8
Typhoid fever.....	3
Cerebral hemorrhage.....	3
Anterior poliomyelitis.....	1
Solitary tubercle.....	1
Cerebellar tumor.....	1
Measles and pneumonia.....	1

It appears from the above considerations, that *without lumbar puncture, a diagnosis of cerebrospinal meningitis is absolutely without value for scientific, statistical, or therapeutic purposes.*

INDICATIONS FOR LUMBAR PUNCTURE.—The importance of an accurate diagnosis in suspected cases of meningitis is so great, that the practical question which confronts the physician in every case is whether or not he should perform lumbar puncture. Naturally one does not wish to perform a useless lumbar puncture in cases of pneumonia or gastro-intestinal disease. On the other hand, I believe that any physician is seriously to be blamed if a case of meningitis does not receive early diagnosis and proper treatment. In every case in which any of the symptoms described above as being characteristic of meningitis are present, the possibility of this diagnosis should be recognized. The indications for lumbar puncture in such cases may be summarized as follows:

If, as a result of a careful history and physical examination, the physician can find definite evidence of the existence of another disease process capable of producing the meningeal symptoms, he is justified in regarding this condition as the cause of the symptoms, and lumbar puncture is not indicated. If, on the other hand, the physician cannot find satisfactory evidence of any other disease process capable of producing the meningeal symptoms, immediate lumbar puncture is indicated.

If the fluid obtained by lumbar puncture be absolutely clear, epidemic cerebrospinal meningitis can be positively excluded, except in cases which have run so long a course as to be already in the late chronic stage. If the fluid be cloudy, the physician can conclude that some form of meningitis is present, and as the form caused by the meningococcus is the commonest which produces cloudy fluid in children, it is best to conclude that the case is one of this type. If the fluid be blood-stained, no positive conclusion can be drawn. The final positive diagnosis depends upon the results of the laboratory examination of the cerebrospinal fluid, the technic of which has been thoroughly described in Division II. For a positive diagnosis, it is essential that the *diplococcus intracellularis* be found in the fluid. If, however, there is a marked predominance of polymorphonuclear cells but no organism of any kind is found, it is best also to assume for therapeutic purposes, that the case is one of epidemic meningitis.

PROGNOSIS.—Before the days of antimeningitis serum, the prognosis varied with different epidemics. The mortality at different times and in different localities has ranged from 50 per cent to 100 per cent, the average mortality being about 70 per cent. In cases which recovered, serious and permanent sequelae were observed in more than 25 per cent. Since the introduction of serum therapy the

mortality has been very much reduced, and in 1300 serum treated cases reported by Flexner, it was 30 per cent. The frequency of occurrence of serious complications and sequelae has also been greatly reduced by serum treatment.

This great reduction in the mortality of the disease effected by serum treatment has been mainly observed in the cases which occurred during recognized epidemics. In my experience, when the disease is epidemic, or even prevalent, the prospect of a good result from serum treatment is very much better than in the sporadic cases which occur occasionally when the disease is not prevalent. For example, the disease was prevalent in Boston and vicinity in 1907-8, the first year that serum treatment was used here. Since then, the prevalence of the disease in Boston has been steadily diminishing from year to year. In 1907-8 I administered serum to sixty-two cases with a mortality of only 20 per cent. Since this time I have seen a decreasing number of cases each year with a continuous increase in the mortality of the serum treated cases; and in 1914-15 I administered serum to only four cases with a mortality of 50 per cent. It is probable that the cases which occur sporadically, when the disease is not epidemic, are likely to be due to resistant or "fast" strains of diplococci, and that this accounts for the relative lack of effectiveness of serum therapy.

In considering the prognosis in a single case, various circumstances must be taken into consideration. In the first place, if the disease is epidemic, the outlook with early serum treatment is decidedly good. If, on the other hand, the case is a sporadic one, the outlook even with early serum treatment is very doubtful. The prognosis also depends on the age of the patient, the severity of the case, the period in the disease at which serum treatment is begun, and the skill with which the treatment is directed. The fatality of the disease varies directly with the age of the patient. Previous to the use of serum, the mortality in infants under two years of age was 100 per cent. In Flexner's series the mortality in infants in the first year was 89 per cent, and in infants under two years, 83 per cent. The severity of the case can be fairly well estimated by the character of the symptoms which appear in the first two or three days. The fulminating type is practically always fatal, and severe cases can only occasionally be saved by early serum treatment. In the other types the outlook is better. The earlier in the course of the disease that the serum is given, the better are the prospects of recovery. In cases which have advanced into the late chronic stage of the disease, and in which no organisms are found in the cerebrospinal fluid, the outlook is bad and no good result is to be expected from serum treatment. In any case, however, in which organisms are still present in the cerebrospinal fluid, there is a prospect of obtaining a good result

from the use of serum. The prognosis in such cases depends mainly upon how much damage has been done to the tissues in the period before the serum is first given.

TREATMENT. INDICATIONS FOR SERUM THERAPY.—The administration of antimeningitis serum is indicated in every case of epidemic cerebrospinal meningitis, except those cases which have advanced so far into the chronic stage of the disease that the meningococcus is no longer present in the cerebrospinal fluid obtained by lumbar puncture. If the physician has no serum at hand at the time when he makes his first diagnostic lumbar puncture, he must perforce wait until he can obtain the serum, and will have time to confirm the diagnosis by the laboratory examination of the cerebrospinal fluid. Whenever it is possible, however, it is best for the physician who is called to see a suspected case of meningitis to carry the serum with him, so that he can administer a dose at the time of the first lumbar puncture. It is true that at this time the diagnosis cannot be positively confirmed, but so important is the early administration of the serum, that there are certain conditions which warrant its immediate use even before the laboratory examination of the cerebrospinal fluid is made. The indications for giving the serum at the time of the first lumbar puncture are the following:

1. If the fluid obtained by lumbar puncture shows any cloudiness without being blood-stained.
2. When, with blood-stained fluid, the patient is severely ill with symptoms strongly suggestive of meningitis.

With either of these conditions the immediate administration of serum is warranted without waiting for the results of bacteriological examination. Further injections, of course, are only to be given in case the laboratory examination of the cerebrospinal fluid confirms the diagnosis by revealing the presence of the diplococcus intracellularis. When the serum is not at hand at the time of the first visit, if the laboratory examination of the fluid confirms the diagnosis, serum should be obtained and used as soon as possible.

TECHNIC FOR THE ADMINISTRATION OF ANTIMENINGITIS SERUM.—The antimeningitis serum is injected directly into the spinal canal. All the evidence goes to show that the subcutaneous injection of the serum is practically of no value in comparison with the subdural method.

The technic of lumbar puncture has been described in Division II. When serum is to be administered, as much fluid as possible should be allowed to escape. The withdrawal should be continued until the fluid is running no faster than four drops to the minute. While the fluid is running, a sterile syringe should be filled with the proper dose of serum, which has previously been warmed to about blood

temperature. The needle remains in place. After the air is expelled from the syringe, the latter is connected with the needle, and the serum is injected through the same needle by which the spinal fluid has escaped. The injection should be made slowly, so as to consume about the same amount of time as that taken by the fluid in escaping. During the injection the patient should be closely observed, particularly as to respiration, pulse, and color. Signs of dangerous rising of the intradural pressure are very rare, but are occasionally seen, and should be watched for. As I have seen them, these signs occur in the following order; disturbed or stertorous respiration, cyanosis, cold sweat, and failing pulse. When they appear, the syringe should be disconnected, and the serum should be allowed to run out again through the needle until these symptoms have disappeared. I am in the habit, after finishing the injection of serum,

FIG. 147



Injection of serum into spinal canal

of holding the needle and syringe in place for three or four minutes before withdrawing the needle. This does away with the necessity of making a second puncture in case pressure symptoms appear. A few patients complain of pain, either in the head or along the course of the sciatic nerves, during the injection of the serum. Sciatic pain may be due to failure to have the serum warmed before it is injected. Neither form of pain is a contraindication to injection, as neither lasts long.

After the withdrawal of the needle, the puncture is covered with a little piece of sterile absorbent cotton held in place by collodion.

THE DOSES OF SERUM; REPEATING THE INJECTIONS.—The follow-

ing is a condensation of the method to be employed in the routine treatment of epidemic cerebrospinal meningitis with serum:

1. When lumbar puncture is performed in a suspicious case, be prepared to inject the serum. If the cerebrospinal fluid withdrawn is cloudy, make the injection of serum immediately and without waiting for a bacteriologic examination. The next doses of the serum are to be given only if the *diplococcus intracellularis* has been demonstrated.

2. Always withdraw as much cerebrospinal fluid as possible at each puncture and inject full doses of the serum. Thirty c.c. of serum should be injected in every instance in which this quantity of fluid or less has been removed, unless a distinctly abnormal sense of resistance in the spinal canal is encountered after as much serum has been injected as fluid has been removed. When the amount of fluid withdrawn exceeds 30 c.c., introduce a larger quantity of serum,—up to 45 c.c., or even more. In the very severe or fulminating cases inject from 30 to 45 c.c. of serum without reference to the quantity of fluid removed unless abnormal resistance is encountered.

3. In very severe or fulminating cases repeat the injection of serum within the twenty-four hour period, as soon as the symptoms intensify, or, when the condition remains stationary, after the lapse of the first twelve hours.

4. In cases of average severity make daily injections of full doses for four days. If diplococci persist after the fourth dose, continue the injections until they have disappeared.

5. If the subjective symptoms including fever and mental impairment persist after the diplococci have disappeared, or after the four doses have been given, and improvement is not progressing, wait four days, if the condition is stationary, and then repeat the four injections. Should the symptoms have become worse before the expiration of this period, the injections should be resumed immediately.

6. In relapse, which is indicated either by reappearance of the diplococci in the cerebrospinal fluid or recrudescence of the symptoms, the four doses at twenty-four hour intervals are to be repeated and the subsequent treatment is to be conducted as for the original attack.

7. This plan of treatment is to be followed until the patient is free from symptoms, the diplococci disappear from the cerebrospinal fluid, or the chronic stage of the disease supervenes. The serum has proved of some benefit in the chronic stages in which the diplococci are still present in the meninges. When the condition of hydrocephalus has been established the injection of serum into the spinal canal promises little.

EFFECTS OF SERUM TREATMENT.—In the most favorable cases the administration of antimenigitis serum produces a very striking effect upon the symptoms of the disease. Often after a single dose there is a fall of temperature and an improvement in the symptoms. In some cases the fall of temperature amounts to a permanent crisis; in other cases a fall by lysis occupying only two or three days, is seen. The symptoms which are first relieved are the clouding of the mentality, and such subjective symptoms as headache, hyperesthesia, and tenderness of the neck. The rigidity of the neck and Kernig's sign are always much more persistent. This most favorable action of the serum is most often seen in cases occurring in epidemics in which the serum is given early.

In other cases, the effect of the serum upon the temperature and symptoms is just as marked, but is not so immediately apparent, often not appearing until two or three injections have been given. In all these favorable cases the duration of active symptoms is cut down to not more than one week.

In some cases, seen more often when the serum is given late, or in sporadic cases, the effect of the serum is not so apparent, and the disease continues to run a rather long course with gradual if any improvement.

Another notable effect of the serum is seen in the successive examinations of the cerebrospinal fluid during the period of its use. This effect is most striking in early cases, in which the cerebrospinal fluid contains large numbers of diplococci. In such a case a great many extracellular diplococci are observed in the fluid withdrawn by the first lumbar puncture. Twenty-four hours after the first injection, the fluid presents a strikingly different picture. The whole number of organisms seen is much smaller, but the chief change is that the majority are intracellular, only rare extracellular forms being seen. The third lumbar puncture shows still fewer diplococci, and those only intracellular. In the fourth fluid, after three doses, there are frequently no diplococci to be found, or, at most, very rare intracellular forms.

DIFFICULT AND RESISTANT CASES.—A certain number of cases are resistant to serum therapy. In some of these the trouble is due to some difficulty which arises in the administration of the serum; in others the trouble is due to various causes within the body of the patient. These resistant cases may be classified under the following three types: (1) Cases in which cerebrospinal fluid cannot be obtained by lumbar puncture; (2) cases in which serum therapy causes disappearance of the meningococci from the cerebrospinal fluid, but does not cause relief of symptoms; (3) cases in which serum therapy produces neither relief of symptoms nor disappearance of the organisms from the cerebrospinal fluid.

In the majority of cases cerebrospinal fluid can be obtained at each lumbar puncture. Occasionally, however, most often in infants, in spite of the most careful technic, lumbar puncture results in a dry tap. When a dry tap is obtained at the first diagnostic lumbar puncture, not only can serum therapy not be employed, because there is no assurance that the serum is going into the cerebrospinal canal, but even the diagnosis is left in doubt. In such cases the physician can only repeat the lumbar puncture in the hope of subsequently obtaining fluid. In the meantime no specific therapy can be used and the treatment must be wholly symptomatic. Usually, however,

FIG. 148



Tapping the cerebral ventricle

dry taps are not encountered until later in the treatment of the case, and the physician is proceeding under the assurance that the diagnosis of epidemic meningitis has been established. Intraspinous injections of serum in such cases are apt to be of no use, because if serum can be properly injected into the spinal canal, fluid should be obtained by lumbar puncture. In infants with whom this condition arises, I believe that the physician is justified in undertaking more heroic treatment. The diagnosis of epidemic meningitis having been confirmed, the prognosis in a child under two years is absolutely

unfavorable, and the only hope is from serum therapy. I believe that in such cases the serum should be injected through the anterior fontanelle directly into the cerebral ventricles. There are not enough statistics on the results of this procedure to afford definite evidence as to whether it is of value. Most of the cases in infants in which dry taps have compelled the use of intraventricular injections of serum, have died. Nevertheless one or two of my cases have recovered under this treatment, and I believe it is worth trying in so serious a condition.

FIG. 149



Injection of antimeningitis serum into the cerebral ventricle

In making an intraventricular injection, the same needle is used as that employed for lumbar puncture. The needle is introduced at one of the lateral angles of the anterior fontanelle and is pushed straight downward, that is, in the direction of the patient's feet, care being taken not to incline the needle at all toward the median line, but if anything very slightly outward. The entrance of the needle into the ventricle is betrayed by a spurt of fluid, which is caught in a sterile test tube. The amount of serum which is then injected should be equal to the quantity of fluid withdrawn. These injections may be repeated under the same indications as those for intraspinal injections.

In a certain number of cases the effect of the serum upon the cerebrospinal fluid is shown in the progressive diminution and gradual disappearance of the diplococcus intracellularis in the successive specimens examined. Nevertheless the symptoms of the disease, including the fever, are not notably affected. In such cases it is probable that some mechanical obstacle exists which prevents the serum from reaching the portion of the central nervous system involved in the disease. Some area is probably shut off, and in this area the organisms continue to multiply and to produce symptoms. In one such case I found at autopsy a closure of the foramen of Ma-

FIG. 150



Position of insertion of the needle through the fontanelle in tapping the cerebral ventricles

gendie by scar tissue, and the ventricles thus shut off were full of diplococci. In such a case the intraventricular injection of serum would also be indicated. Whenever this condition of disappearance of the organisms from the cerebrospinal fluid without relief of symptoms occurs in an infant, I believe that the cerebral ventricle should be tapped, and if the fluid thus obtained reveals the presence of the diplococcus intracellularis, serum should be injected into the ventricles. If no organisms are found in the ventricular fluid, nothing further can be done with serum therapy, and vaccine therapy should be employed. In older children in whom this condition arises, intra-

ventricular injections are not warranted, and the only specific treatment available is that with vaccines.

When the intraspinal injections of serum are followed by disappearance of the organism from the cerebrospinal fluid and by a permanent fall in the temperature to the normal, the persistence of other symptoms means that the patient is suffering, not from the results of an active infection, but from the results of the organic damage left behind by the foregoing infection. In other words, the serum has succeeded in stamping out the disease, but the damage to the cerebral tissues is sufficient to cause a continuance of symptoms. In such cases the symptoms may be due to an increased formation of cerebrospinal fluid, which may persist for a considerable time. The proper treatment of this type of case is frequent lumbar puncture, made with the idea of withdrawing the excess of cerebrospinal fluid, and thus relieving the pressure. All specimens of cerebrospinal fluid should be carefully examined for the presence of diplococci, and if at any time organisms should reappear, intraspinal injections of serum should be begun at once, and continued until the disappearance of the organism, or until the physician is convinced that the chronic stage has supervened.

The most resistant type of case is that in which serum therapy produces no appreciable effect either upon the symptoms or upon the organisms in the cerebrospinal fluid. The question arises whether we should continue to give the serum indefinitely in such cases. I believe that if after four to six successive daily injections no effect whatever is observed, there is little good to be expected from continued serum therapy. This type is seen most often in sporadic cases. The probable cause of the condition is that these cases are produced by a resistant or "fast" type of bacillus which is not to be influenced by serum therapy. These cases should be treated as described for the chronic stage.

TREATMENT OF THE CHRONIC STAGE.—The chronic stage of epidemic meningitis is seen in cases in which the disease has existed for a considerable time before serum therapy was instituted, and also in cases which, for one of the reasons given above, are resistant to serum therapy. In this chronic condition the patients continue to have symptoms, and the predominating symptoms are those of intracranial pressure. The pupils are usually dilated, headache is often severe, and clouding of the mentality is more or less marked, according to the severity of the case. Any of the other symptoms of the disease may persist. The temperature is at times normal, at other times irregularly elevated. Lumbar puncture usually yields an excessive quantity of cerebrospinal fluid. The fluid during the course of such a chronic case is usually at times, clear, at other times,

turbid, containing a variable number of cells. While the polynuclear cells usually predominate, there is a greater proportion of mononuclear forms than in the acute stage. The number of meningococci found in the fluid also varies from time to time; some specimens contain a great number of organisms, others contain either no organisms, or very few.

In this condition the principal pathological lesion is hydrocephalus, which is nearly always present in this stage of the disease. Three measures are employed in the treatment of these chronic cases: (1) Lumbar puncture; (2) intraspinal serum injections; (3) vaccine therapy.

Whenever the amount of fluid obtained by lumbar puncture continues to be always very excessive, the puncture should be repeated daily. In cases in which the amount of fluid is not continually excessive, the puncture should be performed at less frequent intervals, the physician being guided by the symptoms shown by the patient, performing the puncture whenever they tend to grow worse.

It is best not to inject serum at each lumbar puncture in this stage of the disease. Serum therapy produces its effect comparatively early, and in these resistant cases more benefit is to be expected from relief of pressure than from the use of serum. It is true that there is evidence that so long as meningococci continue to be present in the cerebrospinal fluid, some benefit is to be expected from the use of serum. Nevertheless I believe that in the first enthusiasm over serum therapy, too frequent injections were made in this chronic stage, and that not enough attention was paid to the treatment of hydrocephalus and to the relief of pressure. It is wise to give an occasional injection of serum so long as organisms are present, but the intervals between the injections should be much longer than in the acute stage of the disease, and at least two out of three punctures should be performed solely for the purpose of relieving pressure without the injection of serum. In my opinion, frequent lumbar puncture is the most important measure in the treatment of the chronic stage of epidemic cerebrospinal meningitis.

In the acute stage of the disease vaccine therapy gives little prospect of success in comparison with serum therapy. When, however, the chronic stage of the disease has developed, I believe that vaccine treatment should be used as a routine. I have seen a number of cases which have proved very resistant to serum therapy but in which vaccine therapy was followed by recovery. An autogenous vaccine prepared from cultures taken from the cerebrospinal fluid of the patient is preferable, and should be used in all cases, if the physician is master of the technic of preparing the vaccine. When autogenous vaccine cannot be used, a stock meningococcus vaccine may be tried. The first dose should be 50,000,000, and the doses should be gradually

increased 50,000,000 at a time until a response is observed. The intervals between the doses always depend largely upon the reaction and response to the injections. As a routine, three-day intervals are satisfactory.

The use of hexamethylenamin has been widely advocated in the treatment of cerebrospinal meningitis. It has a theoretical value in that it is excreted into the cerebrospinal fluid, but as formalin is only liberated in an acid medium, this theoretical value is very doubtful. There is no conclusive clinical evidence of its value in epidemic meningitis, but nevertheless its use is harmless, and I believe there is no reason why it should not be tried. It would have its chief use in resistant cases and in the chronic stage of the disease. It should never, however, be allowed to take the place of serum and vaccine therapy.

GENERAL AND SYMPTOMATIC TREATMENT.—A disease of this character, leading to such severe emaciation through difficult nutrition, vomiting, persistent fever, and probably specific trophic disturbances, requires the most careful nursing. The nourishment of these patients is also of the first importance. Fluid in sufficient quantities is necessary, but it should be remembered that, except in infants, the diet should not consist exclusively of milk. Broths and soft solids which are easily digested should be given in addition. In certain cases the coma is so marked that the patients are unable to swallow, and under these conditions liquids must be given by means of gavage. The tube may be passed either through the nares or through the mouth. I have found that the frequent passage of the tube is apt to set up a catarrhal inflammation of the mucous membrane. On this account it is well to change the method of passing the tube every few days, from the mouth to the nose, and vice versa.

The bowels should be kept freely open by calomel or saline cathartics. If these drugs are vomited, enemata should be employed.

Other general measures which have been recommended are the application of cold to the head, neck, or spine, the employment of baths, and counter-irritation. Concerning the application of cold by means of ice-caps to the head, or ice-bags to the neck and spine, I believe that the proper procedure is to be guided by the sensation of the patient, relinquishing this treatment if it affords no relief or is unpleasant. I believe it to be quite valueless as a means of influencing the pathological processes of the disease. On account of the extreme sensitiveness of the patients, I believe cooling baths should *not* be employed. Warm or hot baths have been highly recommended by some authorities, but I do not think the evidence presented in their favor is sufficiently convincing to warrant their use as a routine measure. As to counter-irritation by means of tincture of iodine, blisters, or the Paquelin cautery applied to the nape of the neck and

along the spine, there is no evidence pointing toward any value in this procedure.

Of the symptoms which call for special treatment, the most prominent one is pain, which when severe requires morphin, sometimes in fairly large doses. Other nervous symptoms, such as delirium or sleeplessness, are treated with bromides, trional, sulphonal, or chloral. Among these drugs, I should place the bromides in the first rank in meningitis.

Spasm or rigidity of the limbs is the second symptom of importance requiring treatment. The bromides are decidedly the best means of combatting this symptom, and should be given in doses sufficiently large to produce a visible result. If the bromide is vomited or is not well taken by mouth, or disturbs digestion, it may be given by rectum. Convulsions also are best met by the administration of bromide, preferably by the rectum. If the convulsions are prolonged, severe, and repeated, chloral should be given by rectum in addition to bromide. At times prolonged severe convulsions require inhalations of ether.

In many cases, stimulants are required at some time in the course of the disease. They are indicated when there is weak, rapid, or irregular pulse, or stertorous respiration. I believe that caffeine is the best drug under these circumstances. At times digitalis or strophanthus produces good results. Strychnin should not be used, except in case of collapse following the administration of the serum. As to alcohol, the weight of modern opinion appears inclined to deny it any stimulant value. Nevertheless, I believe alcohol is frequently a desirable addition to the treatment of cerebrospinal meningitis, particularly in prolonged cases, with marked emaciation. Possibly its value lies in its aiding the nutrition.

For the residual paralysis, which was formerly a common sequel of epidemic meningitis, but which is only rarely seen under serum therapy, massage, warm baths, and friction should be employed; electricity should be used only when all symptoms of central irritation have subsided.

POLIOMYELOENCEPHALITIS

(Infantile Paralysis). (Acute Anterior Poliomyelitis).

This is an acute infectious disease with characteristic lesions in the central nervous system, due to a filterable virus, and occurring both in epidemics and sporadically.

The earliest clinical studies of the disease were those of Heine in 1840, who called it "*infantile spinal paralysis*." Knowledge of its pathological anatomy began with Charcot's observations on the anterior horns of the spinal cord, and it was from these lesions that

the name "*acute anterior poliomyelitis*" was derived. Clinical knowledge of the disease was greatly advanced by the studies of Medin in the Swedish epidemic of 1890, through which it was demonstrated that while the predominating clinical type is spinal, there are also cerebral, bulbar, polyneuritic, and ataxic clinical types which are evidently due to the same virus. Wickmann's studies in an epidemic in Sweden in 1905-6, demonstrated the existence of clinical types resembling meningitis and Landry's paralysis, and also of an abortive form. At about the same time numerous contributions to the study of the pathological anatomy of the disease demonstrated that in these various clinical forms the distribution of the characteristic lesions in the central nervous system corresponds to the symptoms, and is not necessarily confined to the spinal cord. It is for this reason that the term *poliomyeloencephalitis* is chosen here as being more descriptive of the essential lesions of the infection than is *poliomyelitis*. The term infantile paralysis is open to the obvious objection that the disease is not confined to infancy, nor is it the only form of paralysis seen in infants.

The experimental study of the disease was begun in 1908, when Landsteiner and Poffer succeeded in infecting monkeys by intraperitoneal injection of a preparation of the diseased spinal cord. In 1909 Flexner and Lewis showed that the disease is most easily transmitted to monkeys by intracranial injections, and that it can be thus passed from monkey to monkey. This work, corroborated by other observers, led to a series of experimental studies, upon which is based our present knowledge of the etiology of the disease.

ETIOLOGY. THE MICROÖRGANISM.—Poliomyeloencephalitis is caused by a filterable virus. The proof of this is that an extract of the nervous system of an infected human being or animal can, after filtration through a porcelain filter, infect monkeys.

The virus resembles that of rabies and vaccinia in being very resistant to glycerin. It also stands cold well, retaining its virulence when kept frozen for a number of days. It is killed after heating for half an hour at 55° C. It resists drying. It can live for some time outside the body.

In 1913 Flexner and Noguchi succeeded in growing the virus in a specially prepared anaerobic culture medium, in which the colonies appear as a turbidity of the medium. When the cultures are stained by special methods, a very minute organism is seen, having a diameter of about 0.2 μ . The organisms are rounded-oval bodies occurring singly, in pairs, and in chains. Monkeys inoculated with artificial cultures, even after many generations of cultivation, developed the disease. The minute parasite has been demonstrated in sections of the nervous tissues of monkeys thus infected.

In infected human beings and monkeys, the virus is present in the nervous tissues, in the mesenteric lymph nodes, and in the tonsils and throat. It has a strong elective affinity for the tissues of the nervous and lymphatic systems, and is highly concentrated in the former. The virus in human beings is not present either in the blood or in the cerebrospinal fluid, but has been found in the blood of experimentally infected monkeys. It has been demonstrated in the throats of healthy persons who have been in contact with poliomyeloencephalitis patients, and it is probable that it can exist in a virulent state for a long period in such virus carriers. Carriers, are, however, not common.

TRANSMISSION.—The mode of transmission at the present writing, (February first, 1917) is still unknown. There is probably little doubt that every case of the disease comes from some preëxisting human case. The principal obstacle encountered in studying the mode of transmission, is the fact that the *portal of entry* for the virus has not been ascertained. The virus can leave the body in the secretions from the buccal and nasal cavities, and the presence of the virus in these cavities suggests that the portal of entry may be the lymphatics of the pharynx. This theory has not been proven, although some attempts to infect monkeys by scarification and inoculation of the pharyngeal mucosa have succeeded.

Two theories are held as to the mode of transmission in poliomyeloencephalitis:

1. The first theory is that the disease is spread by *personal contact*. The low contagiousness of the disease suggests that the contact is more often indirect than direct. The demonstration of virus carriers suggests that the means of transmission in indirect contact is probably a healthy person, but in view of the longevity of the virus outside the body, transmission by contaminated objects remains a possibility.

2. The second theory is that the disease is transmitted by means of *insects*.

Neither of these theories has been conclusively proven to be true. The evidence for and against each theory will be reviewed under Problems and Research.

Whether the theory of personal contact is true or not, it is a fact that the disease is not very contagious. It is very rare that a case of poliomyeloencephalitis can be directly traced to a preëxisting case. The distribution of cases in epidemics, in which the country districts and thinly populated areas often show a greater prevalence of the disease than the densely populated centers, is suggestive of a low degree of contagiousness. More than one case in a family is uncommon, and when such instances do occur, both children are

usually simultaneously affected. There is no tendency to infection among physicians, nurses, and laboratory experimenters working with the disease. Until very recently, in both the Children's and Infants' Hospitals in Boston, cases of poliomyeloencephalitis in the acute stage have not been isolated, and there has never been an instance of transmission in either hospital.

PREDISPOSITION.—The general susceptibility of human beings toward poliomyeloencephalitis cannot be determined, because of the unknown facts connected with the transmission of the disease. Children are very much more commonly affected than are adults, and this cannot be explained on the ground of immunity acquired in childhood, as the disease is not common enough for such an explanation. There must be an actual increased susceptibility in early life. The disease is commonest at the age of from one to three years, but often occurs both in very young infants and in older children. It can also occur in adults, but is rare. Race has no effect on predisposition.

There is a very marked seasonal incidence in poliomyeloencephalitis. The disease is usually most prevalent in the months of August and September, and most of the pronounced epidemics have occurred in summer. Occasional cases and small epidemics have been seen at other seasons.

IMMUNITY.—An attack of poliomyeloencephalitis confers a high degree of immunity. Second attacks are practically unknown. The blood serum of individuals who have had the disease will neutralize fatal doses of the virus in the monkey. This principle has been used in two ways: First to confirm the clinical diagnosis in abortive cases; second, as a means of specific therapy. Monkeys that have recovered from experimental infection cannot be reinfected. Owing to the marked predisposition toward the disease in the earlier years of childhood, and the lessened susceptibility in later life, it is impossible to determine how long immunity persists. The fact that localities which have experienced an epidemic are often singularly free from the disease in the next succeeding years, has been attributed to acquired immunity. I do not think that this is a correct explanation, for even if the existence of many abortive cases be granted, the disease does not affect a sufficiently large proportion of the population, and there are many susceptible babies. The freedom from disease of certain localities, both during and after an epidemic, can be better explained upon the basis of the unknown features in the transmission of the disease.

EPIDEMIOLOGY.—The sporadic occurrence of poliomyeloencephalitis has been known for over a century, but widespread epidemics apparently did not occur until within the last thirty years. Until 1907, the large epidemics were confined to Scandinavian countries,

but since 1907 they have been seen in most civilized countries. There were 6,000 cases in the Swedish epidemic of 1911.

In this country the disease has, since 1907, been epidemic every summer in some part of the country. Some of these epidemics have been confined to comparatively limited localities, or to the country districts. Others affect a certain city and its surroundings. The present epidemic of 1916 in New York, which involved the city and a large part of the state, is the second visitation since 1907. The disease was epidemic in Boston and its vicinity in 1909. Since then there have been several smaller epidemics in other parts of the state. During the year 1916 the disease has been very prevalent in Boston, throughout the State of Massachusetts, and in the adjoining states.

PATHOLOGICAL ANATOMY.—The virus of poliomyeloencephalitis has so marked a predilection for the tissues of the central nervous system, that it is there that the characteristic lesions of the disease are to be sought. The primary lesion is a form of leptomeningitis, and consists in a round cell infiltration, which is most marked in the perivascular lymph spaces of the arteries which enter the tissues of the brain and spinal cord. This perivascular inflammation leads to secondary lesions, such as edema and hemorrhage, in the intima of the vessels. The changes which take place in the nerve tissue proper are secondary to the vascular lesions of the disease, and their severity is determined by the extent and intensity of the vascular involvement. The changes which occur in the nerve cells are essentially degenerative. The reason that the anterior horns of the spinal cord are most involved is, that the arteries which supply them are larger; the reason the cervical and lumbar enlargements of the cord are the most frequent seat of lesions is, that those parts have the most abundant blood supply. Following the degenerative changes in the nerve cells occurs a parenchymatous degeneration of the peripheral fibres. Any part of the central nervous system may be involved in the lesions of poliomyelitis, and the distribution of the process is very variable. It is true that in the majority of cases the spinal cord is the part most involved, but exactly the same pathological changes may be seen in any part of the brain, involving both the gray matter and the white matter. In fatal cases it is usual to find involvement of the entire cord with its pia mater, of the entire medulla oblongata and pons, of the basal ganglia, and often of the cortex of the brain. The extent of involvement of the tissues of the central nervous system is always much greater than would be supposed from the clinical manifestations, and even in comparatively mild cases, extensive areas are affected. It is quite evident from this description that the term *poliomyelitis* is in no way descriptive of the whole extent of the pathological process, and that the term *polio-*

myeloencephalitis is far preferable. Following the degenerative changes in the peripheral nerves there is the usual atrophy of the corresponding voluntary muscles.

SYMPTOMS.—The symptomatology of the disease is, as we should expect from the lesions, very variable and complex. In general, poliomyeloencephalitis presents itself as an acute febrile disease in the course of which a definite paralysis develops. For purposes of description the disease may be divided into stages, and also into clinical types. The division into stages applies to all the clinical types seen. The division into clinical types depends mainly upon the varying distribution of the lesions in the central nervous system. The following are the stages seen in the course of poliomyeloencephalitis:

1. Stage of incubation.
2. Prodromal stage.
3. Acute stage.
4. Paralytic stage.
5. Stage of repair.

The following is Wickman's classification of the clinical types of poliomyeloencephalitis, which is the classification most generally accepted at the present day:

1. Common spinal paralysis; anterior poliomyelitis.
2. Progressive spinal paralysis; Landry's paralysis.
3. Bulbar paralysis.
4. Acute encephalitis.
5. Ataxic form.
6. Polyneuritic form.
7. Meningitic form.
8. Abortive form.

STAGE OF INCUBATION.—The duration of the stage of incubation in human beings cannot be determined with certainty, because in most cases the exact time when the infection is acquired is unknown. It probably varies from five to ten days, averaging one week. Exceptionally it may be shorter or longer than these limits. In monkeys it averages about ten days, but much longer periods have been observed at times.

THE PRODROMAL STAGE.—This stage includes the period which elapses from the first appearance of symptoms of any kind until the beginning of the fever. In the majority of cases there are no prodromal symptoms, and hence no prodromal stage; this is particularly true of the common spinal type. In some cases prodromal symptoms are seen, the most noteworthy being *irritability, restlessness, apathy, and pain in the spinal region or extremities.*

THE ACUTE STAGE.—The onset of the disease is sudden and in general resembles the onset of any acute infection, such as tonsillitis or influenza. The duration of the acute stage, that is, the period of fever and acute symptoms, is from one to seven days. In the great majority of cases paralysis appears at some time in the first three days. The acute stage really overlaps the paralytic stage, because it is considered to last as long as the fever, which usually persists from two to seven days.

The symptoms of the acute stage are very variable. In some cases nothing is observed except the most usual symptoms of an acute infection such as fever, loss of appetite, and apathy or irritability. At the other extreme in the symptomatology of the acute stage, is seen a clinical picture which much resembles that of meningitis. There are all sorts of gradations between.

In general, the symptoms of the acute stage may be subdivided into three groups: 1. Symptoms which are manifestations merely of general infection without definite connection with the part of the body involved. 2. Symptoms of meningeal irritation. 3. Symptoms due to the affection of the nerve cells, namely, the paralytic symptoms.

The most common symptoms in the first group are the following: *Fever, vomiting, restlessness, apathy, and general muscular weakness.* The most common symptoms in the second group, those of meningeal irritation, are *headache, rigidity of the neck, delirium, stupor, convulsions, photophobia, dysphagia, sluggish pupils, general pain, pain on motion or hyperesthesia, and cold extremities.* The symptoms of the third group are, *paralysis* and the attendant disturbance of the reflexes. These will be described under the *paralytic stage*.

It must be remembered that no symptom or group of symptoms is in any way characteristic of the disease. The symptoms enumerated above may all be present or absent, and when present may exist in every possible combination. In the majority of cases, before the appearance of paralysis, the physician is confronted by certain symptoms suggesting only an acute infection, possibly with meningeal irritation. The duration of these symptoms is usually not over a week, but may not be more than twenty-four hours. The temperature varies from 100° to 106° , and the fever curve is in no way characteristic.

THE PARALYTIC STAGE.—During the acute stage of the disease, in all but the abortive type to be described below, signs of paralysis of the voluntary muscles appear. The period at which paralysis is first manifest is very variable; it may appear at any time in the course of the acute stage from the first to the seventh day. In my experience, it usually appears within the first three days. It is rather

characteristic of the paralysis in poliomyeloencephalitis that in the majority of cases it assumes its full development almost immediately upon its appearance, but there are certain clinical types in which a progressive form is observed. The various clinical pictures seen with the varying distribution of the paralysis will be described below under clinical types of the disease. In general, the paralysis is usually of the flaccid type with loss of deep reflexes, and reaction of degeneration at the end of a week, the only exception being in the encephalitic type of the disease.

The paralytic stage may be regarded as lasting from the time of the appearance of the paralysis until the beginning of signs of improvement.

THE STAGE OF REPAIR.—The duration of the paralytic stage is very variable. Sometimes the improvement begins almost immediately after the appearance of the paralysis. In other cases improvement does not begin for a considerable time. The stage of repair, however, nearly always begins before the expiration of six weeks. The improvement is usually very marked in the first few weeks after the appearance of paralysis. Usually paralysis disappears completely in certain muscles; residual paralyses become concentrated in certain groups of muscles. The stage of repair continues for from one to one and one-half years. During this period degenerative atrophy continues to be marked in the paralyzed muscles, while *contractures* may develop in the antagonistic ones.

THE COMMON SPINAL TYPE.—In this form the general symptoms are apt to be least severe. Indeed, in some cases the symptoms ushering in the acute stage are entirely overlooked, and the first thing noted is the paralysis. In the majority of cases, however, the acute stage is manifested by a set of symptoms which are suggestive simply of any acute infectious disease. Signs of meningeal irritation are uncommon in this type, and the usual history is that the child became suddenly sick and feverish, sometimes with vomiting or disturbance of the bowels, and then in the course of a few days it was noted that he could not move an arm or a leg, or more than one limb.

The paralysis may occur in one leg, one arm, or in two or three or four extremities simultaneously. The lower extremities are involved most frequently, and in them the quadriceps extensor and the peronei are apt to suffer most. The extent of the muscular involvement in any limb is very variable; only one muscle may be involved, or all the muscles of the extremity may be paralyzed. In the upper extremities, the muscles of the shoulder girdle are most frequently involved, but here also the paralysis may have any distribution. With the paralysis in the extremities there may be also paralysis in the

muscles of the neck, abdomen, and back. It must be remembered also that at times there is paralysis in the neck, abdomen, and back, without paralysis of the extremities, and that only single muscles may be involved. When the deep muscles of the neck are affected, the child is unable to hold up its head. When the accessory muscles of respiration are affected the breathing is wholly diaphragmatic. Paralysis of the diaphragm is rare in this type.

FIG. 151



Anterior poliomyelitis
Left leg
Female, 9 years old



Anterior poliomyelitis
Abdominal muscles, left side
Female, 2½ years old

The paralysis in this form of the disease is characteristic of that due to a lesion of the lower motor neuron, and is accompanied by loss of the deep reflexes and flaccidity, and is followed by the reaction of degeneration and muscular atrophy.

In the great majority of cases of this type, the maximum disability

is observed at the time of the first appearance of the paralysis, and the process is not progressive. It is for this reason that the prognosis as to life is good in common spinal paralysis, because in poliomyelencephalitis death occurs from respiratory paralysis, which is produced by an extension of the process to the diaphragmatic center. Occasionally however, there may be during the acute stage in this type of the disease, an extension of the process. I have never seen this occur when the paralysis was confined to the lower extremities, but have occasionally seen it in cases in which the muscles of the shoulder girdle, particularly the trapezius and the deltoid, were involved.

THE PROGRESSIVE TYPE; LANDRY'S PARALYSIS.—This is a very acute form of the disease in which the process usually *extends upward* through the spinal cord, although rare cases have been observed in which there was a downward extension of the paralysis. Any of the general symptoms may be observed in the acute stage of the disease, but usually signs of meningeal irritation are not pronounced, and the symptoms are those of a general infection. Pain in the legs, however, is often a marked prodromal or early manifestation of this type. The paralysis usually appears within twelve hours and involves first the lower extremities. It quickly ascends, leading to a complete paralysis of the lower extremities, and then to paralysis of the upper extremities, which soon also becomes complete. The process continues to ascend, involving the medulla and pons. The patient then becomes cyanotic, respiration becomes very difficult, and is wholly diaphragmatic in character, none of the accessory muscles being used. In this stage the patient may be in a stupor, or may be still mentally clear. Finally, as the process involves the diaphragmatic center, the breathing becomes more and more short and gasping, and death occurs from respiratory paralysis. The entire course of the disease is only a few days, usually not more than three. This is the most fatal of all forms of poliomyelencephalitis, and except in the rare descending forms, death invariably occurs.

THE BULBAR TYPE.—Any of the characteristic symptoms enumerated above in the description of the acute stage of the disease may be present in this type. Usually, however, the mental condition remains clear, and the principal signs of meningeal irritation are headache, rigidity of the neck, Kernig's sign, and photophobia. Staggering is sometimes the first symptom noted.

The paralysis involves the cranial nerves, the ones most frequently affected being the oculomotor, facial, and hypoglossal. The symptoms and signs which reveal the presence of the paralysis depend upon the nerve or nerves involved. Paralysis of the facial nerve is shown by a facial paralysis, or by inability to close the eye. Para-

lysis of any of the three oculomotor nerves (third, fourth, and sixth cranial nerves) is shown by strabismus, double vision, and sometimes drooping of the eyelid. The first sign of paralysis of the hypoglossal nerve is usually difficulty in talking, with a "pudding-mouth voice," and, on examination, difficulty in using the tongue is seen. In more marked cases there is difficulty in swallowing, which may be so pronounced that no food can be swallowed. The vagus is less frequently involved, but I have seen cases in which the first symptom was a nasal voice with regurgitation of liquids through the nose from paralysis of the muscles of the pharynx, and also cases in which the first symptom was loss of voice from paralysis of the movements of the vocal cords.

This type may exist alone or with a paralysis of the extremities. In most of the cases of this form which I have seen, the paralysis was either exclusively bulbar, or else only paralysis of the deep muscles of the neck was present in addition. Bulbar paralysis is sometimes fatal from extension downward of the process to the diaphragmatic center. I have never seen a fatal ending in cases characterized by paralysis of the facial and oculomotor nerves without paralysis of the hypoglossal nerve. When the latter nerve is affected, the condition, while often recovered from, is also often fatal. When death does not occur in bulbar paralysis, the prognosis as to complete restoration of function is very favorable.

THE ENCEPHALITIC TYPE.—This form is seen when there is extensive involvement of the cerebrum. The clinical picture is very variable, but in general this type resembles the more acute forms of tuberculous meningitis, which are sometimes seen in infants. The onset is usually with fever and vomiting, after which there is restlessness, delirium, and finally increasing apathy, which may deepen into stupor. Convulsions are not uncommon in this type, and the pupillary reaction is often sluggish. The paralysis is difficult to detect in the cerebral form of poliomyeloencephalitis. It is due to a lesion of the upper motor neuron, and is of the spastic type. Spastic paralysis is difficult to detect on physical examination in infants. The paralysis may not be very marked, and the amount of muscular spasm is very variable. The most careful physical examination may leave the physician in doubt as to whether the spasm which is present is only symptomatic of meningeal irritation, or whether there is actual paralysis. Careful observation on the part of a trained attendant will often reveal that some movements are not properly performed. Nevertheless, this type is extremely difficult of diagnosis, and is often diagnosed as tuberculous meningitis, the true nature of the disease only becoming evident when recovery ensues. Rigidity of the neck and Kernig's sign are usually absent in this form, in contradistinction to the meningitic form described below.

The encephalitic type of the disease is occasionally fatal from coincident involvement of the upper part of the spinal cord. The majority of the cases, however, recover, and repair is usually more complete than in the common spinal form of the disease, so that the prognosis as to eventual complete restoration of function is very good.

THE ATAXIC TYPE.—In this form the clinical picture closely resembles Friedreich's ataxia. It is due to the fact that the lesions of the disease may involve the cerebellum, or the cerebellar paths in the spinal cord, the medulla oblongata, the pons, or the midbrain. The characteristic symptom of the disease is incoördination, which manifests itself in walking, or in the use of any of the voluntary muscles. Many cases which have been described by neurologists as "Acute Ataxia in Children," have probably been instances of the ataxic type of poliomyeloencephalitis. The prognosis of this type is in general good, both as to life and as to restoration of function.

THE POLYNEURITIC TYPE.—In this form of the disease the symptoms are those of a multiple neuritis. Autopsies have revealed that the actual lesions are in the meninges of the spinal cord. Pain is the principal symptom of this form of the disease. The pain is usually referred to the extremities, but may be referred to the joints, or may be very indefinite in its distribution. It is usually most marked in the paralyzed parts. The pain is usually very much aggravated by passive motion of the extremities. There may be tenderness over the nerve trunks, or extreme cutaneous hyperesthesia, and tenderness may be so pronounced as to lead to the diagnosis of rheumatic fever, the paralysis being entirely overlooked.

In addition to the pain, a varying distribution of paralysis develops which resembles that seen in the common spinal type of the disease. The polyneuritic type is really the common spinal type plus pain, tenderness, pain on motion, hyperesthesia, and sometimes even paresthesia. The diagnosis is made more difficult by the fact that the muscles which are not paralyzed are often held rigidly in order to prevent the pain produced by movement of the paralyzed muscles; the consequent combination of flaccidity and rigidity is difficult to detect and easy to overlook. When a certain amount of rigidity is present, the loss of the deep reflexes is an important aid in the diagnosis. The prognosis in this type of the disease, both as to life and as to restoration of function, is the same as in the common spinal form. The pain, however, is apt to persist longer than the usual duration of the acute stage of the disease, and may persist for several weeks.

THE MENINGITIC TYPE.—In this form the signs of meningeal irritation are particularly prominent, and dominate the clinical picture. The onset is usually with fever, headache and vomiting.

Other common symptoms are pain in the back, rigidity of the neck, tenderness of the neck, a tendency to opisthotonos, positive Kernig's sign, photophobia, sluggish pupils and a mental condition varying from delirium to stupor. The clinical picture presented resembles in every way that of epidemic cerebrospinal meningitis. The development of a definite paralysis which may involve any part of the body, is the only clue to the correct diagnosis, and even the presence of paralysis is by no means a positive sign, because it may be present in cerebrospinal meningitis. One point which I have found of value is, that in cerebrospinal meningitis the paralysis is usually shifting and variable from day to day or even from hour to hour, whereas the poliomyeloencephalitis paralysis, once it has developed, is usually constant. Also paralysis is a comparatively rare symptom in the epidemic form of meningitis. The prognosis in this form as in other forms, depends upon whether or not the respiratory centers become involved in the process. The majority of cases of this type recover.

THE ABORTIVE TYPE.—It is very difficult to give a clinical description of the abortive forms of the disease. We know that such forms exist, and in the presence of an epidemic, or of a marked prevalence of the disease, it is sometimes possible to recognize an abortive case. In this type the general symptoms of the disease with all their variations, may be present without the development of paralysis. A good deal has been written about the importance of a triad of early symptoms, namely, sweating, irritability, and hyperesthesia, in the recognition of abortive cases of poliomyeloencephalitis. These symptoms, however, are by no means constant, although their presence is strongly in favor of poliomyeloencephalitis when no other localization for the infectious process can be demonstrated. Their absence does not rule out an abortive form of infantile paralysis. Most cases of the abortive type present a clinical picture which might go with any of the recognized acute infections, and infantile paralysis is usually only suspected because of the presence of an epidemic. The diagnosis, however, can often be confirmed by the results of lumbar puncture.

THE BLOOD.—A good deal has been written about the changes in the blood in poliomyeloencephalitis. Some observers have reported a decrease in the leukocyte count during the acute stage. Others have reported an increase, while still others have reported little or no change. In experimental poliomyeloencephalitis in monkeys, the changes in the blood appear to be more constant. There is a leukopenia, or at any rate, an absence of leukocytosis in the acute stage, with a relative lymphocytosis. The changes in human beings appear to be much less constant and are not sufficiently pronounced to be of practical value in the diagnosis of the disease.

THE CEREBROSPINAL FLUID.—In the acute stage of the disease, there is a constant increase in the number of cells in the cerebrospinal fluid. In the experimental disease of monkeys, this increase in cells begins during the stage of incubation. Cerebrospinal fluid in cases of poliomyelencephalitis, is usually clear and is under increased pressure. A fibrin clot usually forms on standing, but this is sometimes absent. The cell count varies from 30 to 400 cells per cubic millimeter. It usually lies between 75 and 200 cells per cubic millimeter. The majority of the cells, usually about 98 per cent, are small lymphocytes. It is thus apparent that during the acute stage of the disease the cerebrospinal fluid resembles in every way that of tuberculous meningitis, except that tubercle bacilli cannot be demonstrated.

These characteristic appearances in the cerebrospinal fluid are most marked early in the acute stage of the disease. As the acute stage progresses, the fibrin clot quickly disappears, the cell count falls rapidly, the proportion of large mononuclear cells increases, and finally polynuclear forms appear. I have seen some increase in the cell count as late as the eighteenth day of the disease, although usually the cell count falls to normal at the end of the acute stage. I have occasionally seen a normal cell count as early as the sixth day, before the fever had entirely subsided.

DIAGNOSIS. CLINICAL.—The clinical diagnosis of poliomyelencephalitis depends essentially upon the finding of paralysis. Whenever in the course of what is apparently an acute febrile attack a sudden paralysis can be demonstrated, especially if the paralysis be of the flaccid type, the diagnosis of poliomyelencephalitis is warranted. The only other common acute febrile disease in which paralysis occurs is meningitis. The paralysis of meningitis is most commonly of the spastic type, and is rarely so definite and constant in its distribution as in poliomyelencephalitis. Nevertheless, in some cases of the latter disease with marked symptoms of meningeal irritation, a clinical differential diagnosis is either extremely difficult or cannot be made.

The physician should remember the possibility of poliomyelencephalitis whenever confronted by an acute febrile attack in early life. This possibility is strengthened when signs of meningeal irritation are present. The diagnosis can only be confirmed by the detection of the paralysis, and this often requires the most careful physical examination. The physician should, if possible, test the power of every muscle. Particular points to be noted in the physical examination are the following: The movements of the eyeballs; the reactions of the pupils; the movement of the muscles of the face; the character of the voice; the movement of the tongue, and the ability

to swallow both solids and fluids; the character of the respiration, diaphragmatic breathing being particularly significant; the ability of the child to hold up its head; the resistance of the limbs to passive motion, whether characterized by flaccidity or rigidity; the power to perform all the voluntary movements which it is possible to get the child to attempt; the presence or absence of pain on passive motion of the limbs; the character of the reflexes. If all these points be carefully noted, paralysis when present, will not be overlooked.

Whenever the physician is in doubt as to whether or not paralysis is present, the diagnosis in the acute stage of the disease can only be settled by the results of lumbar puncture.

The question arises whether a clinical diagnosis of poliomyeloencephalitis can be made before the appearance of a recognizable paralysis. The answer to this question is most emphatically that a diagnosis based upon the history and physical examination cannot be made. This statement also applies to the diagnosis of the abortive types of the disease. When poliomyeloencephalitis is prevalent, or when an epidemic exists, the physician can often suspect the possibility of poliomyeloencephalitis before the appearance of paralysis, or in abortive cases. He can only confirm his suspicion by the results of lumbar puncture.

LABORATORY DIAGNOSIS.—The examination of the cerebrospinal fluid obtained by lumbar puncture gives the most valuable obtainable evidence in the diagnosis of poliomyeloencephalitis. In the acute stage of the disease, whether or not paralysis has developed, the characteristic appearances in the cerebrospinal fluid are practically constant. The finding of a normal cerebrospinal fluid, that is, a fluid without fibrin formation and with a normal cell count, enables the physician definitely to rule out poliomyeloencephalitis in the acute stage of the disease. When, however, a fibrinous clot and an increase in the number of lymphocytes are found in the cerebrospinal fluid, it means that the case is either one of poliomyeloencephalitis or of tuberculous meningitis. In deciding between these two conditions the physician must be guided by the other clinical features of the case, and by whether or not tubercle bacilli can be demonstrated in the fluid.

The fact that the examination of the cerebrospinal fluid obtained by lumbar puncture is of such great importance in the diagnosis of poliomyeloencephalitis, does not necessarily mean that diagnostic lumbar puncture is indicated in every case. The question must now be considered, what are the indications for diagnostic lumbar puncture in a suspected case of infantile paralysis? If the disease had a thoroughly established specific therapy, the value of which depended upon an early diagnosis, there would be no doubt that diagnostic

lumbar puncture would be indicated in every suspected case of poliomyeloencephalitis, just as it is in every suspected case of epidemic cerebrospinal meningitis. But it is a fact that there is at present no definitely established specific therapy for poliomyeloencephalitis, and consequently it is open to question whether a physician is justified in performing lumbar puncture for diagnostic purposes only, when the making of a positive diagnosis is not essential for proper treatment. It may be argued here that the making of a positive diagnosis is essential for proper prophylaxis in order that cases of poliomyeloencephalitis may be properly isolated, and that adequate precautions may be taken against the spread of the disease. On the other hand, however, it must be remembered that the symptom-complex of poliomyeloencephalitis markedly resembles that of many common acute infections, and if the physician adopted the practice of performing a diagnostic lumbar puncture in every case presenting such a symptom-complex, he would be obliged to perform many entirely superfluous lumbar punctures upon children who are suffering from comparatively trivial affections. Moreover, as far as prophylaxis is concerned, I believe that every acute infectious disease of which the nature is as yet undetermined should be isolated, and that precautions should be taken against its transmission to others, until the true nature of the infection becomes manifest. If this is done, there will be no necessity for diagnostic lumbar puncture for purposes of prophylaxis.

I believe that the decision as to whether or not lumbar puncture shall be performed must depend upon the circumstances of the individual case, and that no routine rule can be given as to the indications for this diagnostic procedure. If in the particular case the circumstances are such as to make a positive diagnosis highly desirable for purposes of prophylaxis or treatment—if for example, the physician is going to try any of the newer methods of specific treatment, the value of which is not definitely proved, if the parents of the patient are strongly desirous of an immediate positive diagnosis, if the patient is in a general hospital ward in which a positive diagnosis is essential for the protection of others—under all these circumstances, diagnostic lumbar puncture is indicated. In private cases, however, in which it is deemed advisable not to try an unproved method of specific treatment, the physician should explain that the results of lumbar puncture are only of value in establishing the diagnosis, that they do not influence the treatment, and that if the patient can be properly isolated, lumbar puncture need not be performed unless the parents insist upon an immediate positive diagnosis.

DIFFERENTIAL DIAGNOSIS.—In the early stages of the disease, poliomyeloencephalitis must be distinguished from the following conditions:

1. *Meningitis*.—Whenever meningeal symptoms are sufficiently pronounced to be compatible with the possibility of epidemic meningitis, diagnostic lumbar puncture is always indicated. This means that lumbar puncture should be performed in the meningitic type of infantile paralysis, and also in all cases which have meningeal symptoms without a paralysis characteristic of poliomyeloencephalitis. It must be remembered, however, that the development of a definite and constant paralysis inclines the diagnosis strongly toward the latter disease, although it is not wholly incompatible with meningitis. The results of lumbar puncture will differentiate clearly between infantile paralysis and all forms of meningitis except the tuberculous.

The distinction between the more acute types of tuberculous meningitis and the encephalitic type of poliomyeloencephalitis is often very difficult. Lumbar puncture does not help here unless the tubercle bacillus is found in the cerebrospinal fluid. But it must be remembered that with ordinary routine methods of examination the bacillus is not found in more than 10 per cent of the cases of tuberculous meningitis. The complete absence of paralysis is in favor of meningitis. In many cases, however, a diagnosis cannot be made except from the outcome of the case.

2. *Other Acute Infections*.—Poliomyeloencephalitis may have the same initial symptoms of these conditions, and the differential diagnosis depends upon the development of paralysis or of the essential signs of some other infection.

Later in the disease, we have to distinguish poliomyeloencephalitis from the following conditions:

3. *Multiple Neuritis*.—This condition is often to be distinguished from the polyneuritic type of the disease. The principal distinguishing points in polyneuritis are the following: The slower development; the paralyzes are not complete at the beginning; objective sensory disturbances are usually more marked and last longer; the paralysis has a peripheral nerve topography rather than a radicular topography, is apt to be more distal in the extremities, and is often bilaterally symmetrical.

4. *Acute Myelitis*.—In this condition the involvement of the pyramidal tracts usually gives a spastic paralysis in the muscles supplied from the cord *below* the site of the lesion, while there is a flaccid paralysis of the muscles supplied from the cord at the site of the lesion. The main differential point, however, is that in transverse myelitis, sensory disturbance—particularly anesthesia—is pronounced in the lower part of the body.

5. *Myatonia Congenita*.—I have seen this condition mistaken for infantile paralysis, on account of the markedly flaccid condition of

the muscles. It is a congenital disease and is not ushered in by an acute febrile attack.

6. *The Paresis of Rickets*.—This condition is non-febrile, has a slower onset, and can usually be recognized through the presence of other rachitic stigmata.

7. *Syphilitic Pseudo-Paralysis*.—This has a slower onset, can usually be demonstrated to be only a pseudo-paralysis, and its nature can be recognized by the presence of other syphilitic stigmata.

PROGNOSIS.—There are two distinct aspects under which the prognosis of poliomyeloencephalitis must be considered. These are, (1) the prognosis as to life, and (2) the prognosis as to restoration of function.

PROGNOSIS AS TO LIFE.—This depends mainly upon the type of the disease which is present. It is hopeless in the progressive type. It is very unfavorable in the lower bulbar type with involvement of the hypoglossal nerve, and it is grave in all cases which, while not definitely of the progressive type, show any tendency to extension of the distribution of the paralysis after its first appearance. It is also grave in the encephalitic type, although many cases recover. The nearer the lesion approaches the diaphragmatic center in the upper part of the cord, the more grave becomes the prognosis. Cases of the spinal type, in which the muscles affected are the deltoid, pectorals, and accessory muscles of respiration, have a serious prognosis. Prognosis as to life is favorable in the common spinal type when the paralysis affects the lower extremities, or when it affects the more distal muscles of the upper extremities. It is also favorable in the ataxic and upper bulbar types.

Unfavorable signs are, disturbance of the respiration and difficulty in phonation and swallowing.

The mortality of the disease varies very greatly in different epidemics. According to Wickman, this variation is from 10 to 42.3 per cent. Death, when it occurs, usually takes place on the fourth or fifth day of the disease. It was formerly believed that poliomyeloencephalitis is rarely fatal; this belief was due to the fact that only the common spinal type was recognized, and that the serious types were taken for cerebrospinal meningitis, Landry's paralysis, and so forth.

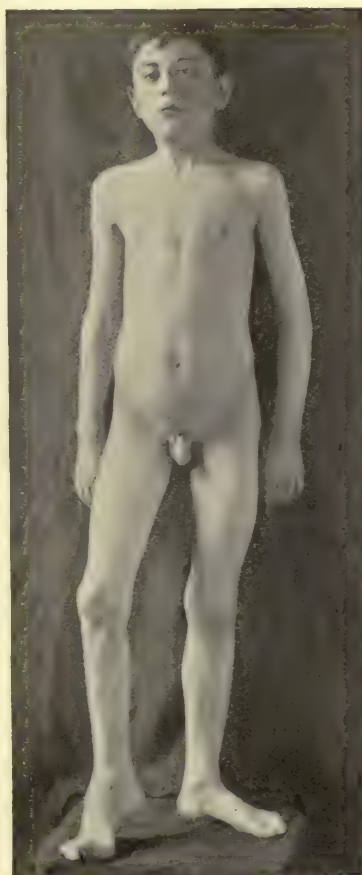
PROGNOSIS AS TO FUNCTION.—It is impossible to give a prognosis as to how complete will be recovery from the paralysis. It is safe to state that some degree of improvement over the initial paralytic condition always occurs. In the amount of improvement, every gradation is seen from very little restoration of function up to complete recovery. While improvement is most marked in the earlier weeks of the stage of repair, it may continue up to two years. Bul-

bar and encephalitic types, while less favorable as to life, are more favorable as to complete restoration of function than is the common spinal type. In most severe cases of the latter, some degree of paralysis, contracture, and deformity, is left behind permanently. Wickman states that complete recovery can be counted on in 20 per cent of the cases suffering from paralysis. In Lovett and Sheppard's series the percentage of complete recovery in the paralyzed cases was 13.5 per cent.

FIG. 152



Anterior poliomyelitis
Flail leg, left side
Male, 6½ years old



Anterior poliomyelitis
Talipes equinus on right side
Male, 11½ years old

PROPHYLAXIS.—It is difficult to prescribe prophylactic measures which should be taken in poliomyeloencephalitis, on account of the unknown features connected with the transmission of the disease. I believe, however, that in a disease with an unknown mode of transmission, every precaution based on the available evidence should be taken. While transmission by personal contact is not

finally proven, there is strong evidence in support of such a theory. Consequently, patients with poliomyeloencephalitis should be quarantined under the same restrictions as are used in diseases which are known to have that mode of transmission. The principal known contact infections are scarlet fever and diphtheria, and therefore the prophylactic measures employed in poliomyeloencephalitis should be exactly the same as are used in those diseases. The only question which arises in this connection is, how long the quarantine should be continued. There are as yet no definite data on this point, and the period of quarantine must be somewhat arbitrary. It would be well if the Board of Health were to set some definite limit for the duration of quarantine. I have personally adopted a period of six weeks, and have as yet had no instance of transmission from one of my patients to another child after the expiration of this period. But further experience may show that six weeks may be either not long enough, or unnecessarily long.

The other children in the family of a poliomyeloencephalitis patient should not be allowed to mingle with their playmates, or to attend school, during the period of quarantine. With our present knowledge, it is hardly necessary to compel the adult members of the family to give up their work or pleasure because of a case of infantile paralysis in the household. They should not, however, be allowed to go about unless they are rigidly excluded from the sick room during the entire period of the quarantine.

The measures which should be taken to prevent the spread of the disease in an epidemic are still a subject of discussion. One of the unsettled questions is, whether or not it is necessary or wise to close the schools, or to delay the opening of the schools, on account of the existence of an epidemic. My own opinion is, that the disease has so little general contagiousness that it is not necessary to close the schools, or to delay their opening. I realize, however, that many authorities differ from me on this point.

Whenever the disease is prevalent, physicians will be constantly asked what measures should be taken to prevent children from acquiring it. At present the general advice which can be given is, that parents should not deliberately take their children to a place where the disease is known to be prevalent. If, for example, my patients are passing the summer in a locality which has been free from the disease, and if the disease is prevalent in the city, I advise them not to bring the children back to the city until the epidemic has subsided. If, however, the epidemic is very widespread, it is probable that no locality is entirely safe, and under such circumstances I have permitted children of school age to be brought back to the city, and to be allowed to go to school. In individual instances it may be wise to advise parents to take their children away from a locality

in which the disease is prevalent, but the danger of infection is hardly great enough to warrant such advice to the community at large.

As to further measures in prophylaxis, there are as yet no very definite data upon which conclusions can be based. There is a possibility, not supported by definite evidence, that hexamethylenamin may prevent the escape of the organism from the body, and it can at least do no harm to give this drug to patients during the acute stage. Similarly, as the nasopharynx may be a portal of entry, hexamethylenamin may be given to those who have been exposed. Weak solutions of peroxide of hydrogen used as a spray in the nose and throat, may have some prophylactic value.

No method of producing an active immunity by vaccine therapy has yet become sufficiently practical to warrant its routine use.

TREATMENT.—At the present writing, no specific method of treatment of poliomyeloencephalitis is generally available. The treatment of the disease must be wholly symptomatic, and in general follows the lines of any acute infectious disease of similar severity. From the first onset of symptoms, patients should be kept in bed. During the acute stage, the management of the diet and nursing is that of any acute infection. Patients should remain in bed for a period of six weeks, and should be kept as immobile as possible. Attempted movements of the paralyzed limbs causes stimulation of the ganglion cells in the cord, and consequently tends to increase the trouble and to interfere with the process of repair. Furthermore, if too much movement be permitted, there is a tendency toward the development of muscular soreness or lameness in the affected muscles, which in children are constantly contracted in the effort to perform impossible movements. If, at the expiration of six weeks, any pain, tenderness, or pain on motion is still present, the patients should continue to remain quiet in bed until three weeks after these symptoms have subsided.

The symptomatic treatment of the acute stage of the disease is very similar to that described for epidemic cerebrospinal meningitis. The principal symptom which requires treatment is pain. Occasionally bromides are required for the relief of muscular spasm or convulsions. Stimulation is of no avail in cases which run an unfavorable course. There is no drug which should be used as a routine during the acute stage of the disease. Hexamethylenamin will do no good after the appearance of the paralysis. Strychnin should be avoided not only during the acute stage of the disease, but also during the period of six weeks' rest which follows the appearance of paralysis. Local applications to the head, neck, or spine, are entirely useless in affecting the course of the disease, and do not add to the comfort of the patient except in a few cases with severe headache.

No active treatment of the paralyzed limbs should be begun for six weeks at least. During this time, electricity and massage should be avoided for the same reasons that lead to the keeping of the parts as quiet as possible. During this period, the important part of the treatment consists in the prevention of contractures, which develop very quickly, and which make the later treatment of the disease much more difficult. A cradle should be used to keep the weight of the bedclothes off the legs. A right-angled splint should be applied, especially if there is toe-drop, to keep the foot in proper position. Whenever there is any tendency toward a constant improper position of any of the limbs, light splints should be applied to correct the beginning contracture. After the expiration of six weeks, or of a longer period at least three weeks of which have been free from any pain and tenderness, the patient may be permitted to use the limbs. At this time the patient should be placed in the hands of a skilled orthopedic surgeon. The further treatment of these cases belongs to the domain of orthopedics and will not be described here.

PROBLEMS AND RESEARCH.—There are two central problems which at the present day are occupying the attention of research workers on poliomyeloencephalitis. The first is the mode of transmission of the disease, with its important bearing upon prophylaxis. The second is the problem of immunity, with its important bearing upon specific therapy.

The evidence bearing on the subject of the portal of entry and mode of transmission in poliomyeloencephalitis is of two kinds, experimental and epidemiological. The definite facts which experimental research has brought forth have already been mentioned.

In order that the reader shall understand the principal significance of the present and future literature of the disease, it is essential that he be familiar with the arguments for and against the two principal theories as to the mode of transmission, namely, the *contact theory* and the *insect theory*. The former is supported mainly by experimental evidence; the latter mainly by epidemiological evidence.

In favor of the theory that the disease is spread by personal contact, whether direct or indirect, is the fact that the virus is demonstrable in the nasopharyngeal secretions of patients and of carriers who have been in contact with the disease. This suggests that the nasopharyngeal mucosa may also be the portal of entry. It has been shown that in the monkey infection can be produced by scarification and inoculation of the nasal mucosa, and also that smaller doses of the virus are required to produce infection in this way than are required when the virus is inoculated into the blood. This does not necessarily prove, however, that the nasopharyngeal mucosa is either the principal or the sole portal of entry in man, although no evidence

has been brought forward to show with certainty that there is any other portal of entry.

There is also some epidemiological evidence in favor of the contact theory based on certain epidemics in which prophylactic measures directed at preventing the distribution of the disease by personal contact, have been followed apparently by an appreciable diminution of the prevalence of the disease and by limitation of its spread.

The following considerations have been brought forward against the theory that the disease is transferred by direct or indirect human contact. In the first place, the nature of the virus differs from that of the diseases known to be spread through personal contact, and through the infected secretions of the mouth and nose. The virus of poliomyeloencephalitis markedly resembles that of rabies, which is present in the saliva and yet which is not transferred from individual to individual, except through the agency of a punctured wound. The second argument against the contact theory, is the summer incidence of the disease. Most diseases spread by personal contact are more prevalent in winter, when the population is most congested in houses, schools, and so forth. The lack of contagiousness of the disease is the strongest point against the contagious theory. In some epidemics the maximum prevalence of the disease has been in the country districts, where personal contact is least intimate. In other epidemics, the statistics showing the distribution and spread of the disease constitute evidence against the contact theory. The immunity of some districts after an epidemic cannot be explained on the ground of immunity acquired through infection of a large proportion of the population, and is an argument in favor of some other means of distribution than that by personal contact.

The following points are in favor of the theory that the disease is transferred by some other agency than human contact, possibly by rodents, by insects, or both. The most important evidence in favor of this theory is the summer incidence of the disease, which is extremely difficult to explain under the human contact theory, but which is strongly suggestive of transfer by insects. Statistical evidence of all kinds has been brought forward in support of one or another rodent or insect, but none of it is finally conclusive.

Against the insect theory is the fact that the virus does not appear to be present in the blood of human beings. This fact, however, does not preclude transmission by means of insects, as they may become contaminated with infected material from the mouth or nose. Transmission by means of the stable fly has never been conclusively proved. The principal argument against the insect theory is, that it is as yet entirely unsupported by experimental evidence.

At the present time we can only conclude that either one of these theories may be the true one as to the mode of transmission of polio-

myeloencephalitis. The research of the next few years will be awaited with great interest. Recently, Dr. Mark Richardson of Boston, has advanced the theory that the disease is transmitted by means of rats, and the fleas which are common parasites of the rats. He has supported this view by much ingenious reasoning and by interesting statistical evidence, which, however, is regarded by most authorities as entirely inconclusive.

THE PROBLEM OF IMMUNITY AND SPECIFIC THERAPY.—It has been demonstrated that the virus of poliomyeloencephalitis produces a marked immunity both in the monkey and in the human being, and that the blood of both monkeys and human beings who have undergone the infection, possesses a protective value in the experimental disease in monkeys. The development of an effective serum therapy in man has been handicapped by the fact that no animal large enough to yield a sufficient quantity of serum for therapeutic use, is susceptible to the virus of poliomyeloencephalitis. Netter was the first to apply the data obtained by experiments on monkeys to the treatment of poliomyeloencephalitis in man. He employed the serum from cases of the disease in which complete recovery from the acute condition had taken place a considerable time previously, even as long as thirty years. This serum was given by intraspinal injections. The serum must of course be sterile, but need not be inactivated. The size of the dose must be determined by the quantity of serum available, the usual doses which have been used ranging from 5 to 20 c.c. Serum obtained from the blood of human convalescents has been employed in a similar way. The evidence of the value of this treatment can only be manifested in checking the progress of the paralysis in progressive types, or in preventing or limiting the paralysis when given very early in the disease. This method of treatment has been employed to some extent in this year's epidemic. The results are suggestive that it may prove of value, but we shall have to await further evidence before we can consider that the value of this method of treatment is proved sufficiently to call for its routine use.

Various suggestions have been made as to prophylactic vaccination in patients who have been exposed, or during epidemics. The virus is so resistant that the method of immunization employed in rabies cannot be devoid of danger. The best prospects for prophylactic inoculation appear to lie in some such method as that suggested by Römer, in which a preparation of the virus neutralized by immune serum is used as the agent which produces artificial immunity.

V. DISEASES OF DOUBTFULLY SPECIFIC CAUSE

This group includes two diseases in which the causative micro-organism is a *streptococcus*. As the streptococcus can cause a great variety of pathological processes in various parts of the body, with lesions which are in no way specific, it is doubtful whether any disease produced by this organism can be considered a *specific* infection in the strictest sense of the term. The tendency of modern research, however, is to regard the streptococcus as representing not a single type of organism, but a group which includes many *strains* or varieties with differing virulence and pathogenic peculiarities. If rheumatic fever and erysipelas are eventually shown to be due to special varieties in the streptococcus group which produce only the peculiar manifestations of these two diseases, they will rightly be regarded as specific infections.

RHEUMATIC FEVER

(Acute Articular Rheumatism). (Polyarthritidis Rheumatica Acuta).
(Inflammatory Rheumatism).

Rheumatic fever is an acute, non-contagious, infectious disease, characterized by inflammatory non-suppurating lesions in the heart and joints. The term "acute articular rheumatism" used in most text books to describe the disease is based on the pathology of the disease as it occurs in adults, in whom the manifestations are primarily and chiefly articular, the cardiac lesions appearing as complications. It is a bad term for the disease as it occurs in children, in whom the manifestations of the disease are not primarily nor chiefly articular. The term rheumatism is further objectionable in having too wide and ill-defined a signification. From the orthopedic surgeons has come the term "infectious arthritis" as describing the articular lesions of rheumatic fever. The orthopedists, however, are interested in the classification of articular lesions only, and while the articular lesions of this disease belong in the general group of infectious arthritis, rheumatic fever is not chiefly or exclusively a disease of the joints, but gives a clinical picture suggestive of a specific infection of which arthritis is only one manifestation. The term rheumatic fever is used here to describe such a presumably specific infection, the word rheumatic denoting no special theory of etiology, but being used for convenience in the same way as scarlet fever and typhoid fever are used to describe similar infections.

Rheumatic fever occurs with approximately equal frequency in children and in adults. It is, however, a disease that differs widely

in its clinical manifestations and phenomena as we pass from earlier to later childhood, from childhood to adolescence, and again into adult life. I know of no disease common to children and adults which presents such a surprisingly different clinical picture at these two ages. I find that in beginning to demonstrate cases of rheumatic fever in childhood to students whose previous training has been confined to adults, its peculiarities impress them like the revelation of an entirely new disease.

In the adult, rheumatic fever presents itself as an acute disease characterized by inflammation in the joints, with its severe symptoms referable to the joints and with a tendency to cardiac complications of comparatively slight clinical significance in their immediate result. In the child, rheumatic fever presents itself as an acute disease characterized by inflammation in the heart and joints, or both, with its severe symptoms referable to the heart, and with a tendency to arthritic symptoms of comparatively slight clinical significance. This is the principal contrast, stated in its broadest form. In a more detailed view of the disease in childhood many further points of contrast, of great interest, are encountered.

ETIOLOGY. THE MICROÖRGANISM.—While the clinical evidence in favor of the infectious character of rheumatic fever has always been quite convincing, there have until recently been many flaws in the scientific evidence. The various theories which have been held, and the experimental work which has led to the view of the etiology of rheumatic fever advanced here, will be discussed under Problems and Research.

Rheumatic fever is due to a *streptococcus*. The work of Rosenow affords conclusive proof of this. It is known that there are many varieties or strains included in the streptococcus group. The streptococci which cause rheumatic fever have certain peculiar properties. Culturally they differ in various respects from the streptococci associated with the various suppurative processes (the streptococcus hemolyticus) and from the streptococcus viridans found in subacute infectious endocarditis. Furthermore, they produce in animals lesions characteristic of rheumatic fever. In this sense, the streptococcus producing rheumatic fever may be considered a specific variety. Whether or not there are one or more strains of the rheumatic fever streptococci, and the relation of the rheumatic strains to other varieties of streptococci, will be discussed under Problems and Research.

As the disease has specific lesions, and as a variety of streptococcus is associated with the lesions, and reproduces the same lesions in animals, rheumatic fever may be considered a specific infectious disease.

PORTAL OF ENTRY AND TRANSMISSION.—There is abundant evidence that the portal of entry for the rheumatic fever streptococcus is the tonsils. The frequency of the association of tonsillitis and rheumatic fever has long been a recognized clinical observation. Furthermore, streptococci showing all the peculiar properties of the rheumatic fever organisms, have been frequently isolated from the tonsils of rheumatic fever patients. Except in certain rare instances, the organisms are not found in other possible portals of entry. Tonsillitis is so frequently associated with rheumatic fever, that it may be considered one of the clinical manifestations of the disease.

Transmission from one patient to another appears to play practically no rôle in rheumatic fever. The streptococcus is a micro-organism of such wide distribution, that direct transmission and contagion are entirely unnecessary in explaining the occurrence of infection. We must look to other factors, among which are factors affecting the virulence of the streptococci, and factors affecting the constitutional resistance of the individual. The view of Rosenow that the virulence of streptococci, and their affinity for various parts of the body may be altered by various factors, such as symbiosis with other bacteria, and variations in oxygen pressure, and that the tonsils are an especially favorable place for the action of such factors, is very suggestive, and will be discussed under Problems and Research.

PREDISPOSITION.—That there is an important *constitutional factor* in the occurrence of infection with rheumatic fever is suggested by various clinical features of the disease. Prominent among these is the tendency of the disease to recur frequently in the same individual. There is abundant clinical evidence of the importance of *heredity* as an etiological factor.

In addition to a permanent constitutional factor in etiology, it is probable that there are a number of etiological factors predisposing toward infection which act from outside the body. Among such possible predisposing causes are damp dwellings, exposure to cold and wet, poor hygienic surroundings, and insufficient food. The disease occurs at all seasons, but is most common in the spring months. Children are infected with rheumatic fever fully as frequently as are adults. The disease is very uncommon under the age of five years, and is so extremely rare in infancy as to be almost unknown. After the fifth year the disease is seen with increasing frequency, and in the years preceding puberty it is somewhat more common than in adult life. The explanation of the immunity of infancy and early childhood, is unknown. It may be constitutional, or may depend on local conditions in the throat.

IMMUNITY.—There is no evidence of any lasting immunity con-

ferred by an attack of rheumatic fever. Nothing is known of the mechanism by which recovery takes place.

PATHOLOGICAL ANATOMY.—The organisms of rheumatic fever produce lesions in various parts of the body. It is quite possible that the parts of the body involved in different cases are, as suggested by Rosenow, due to differing affinities of various strains of the rheumatic fever streptococcus.

The principal affinity of the rheumatic fever streptococcus is for the *heart*, and for the synovial membrane of the *joints*. The other serous membranes, *pleura* and *peritoneum*, are occasionally affected. Acute non-suppurative *myositis* is sometimes a manifestation of rheumatic fever, although most of the cases clinically described as muscular rheumatism are not instances of rheumatic fever infection. The rheumatic fever organism may also cause characteristic lesions in the skin, the so-called *subcutaneous nodules*.

The lesion of the joints is a non-suppurative synovitis in which nothing especially characteristic of the disease has been demonstrated. Also the lesions of the pleura and peritoneum have not been shown to be specific, being ordinary fibrinous, serous, or sero-fibrinous inflammations.

In the *heart*, however, the lesions of rheumatic fever are characteristic. The essential lesions have been called by Coombs "sub-miliary nodules." These lesions consist of a groundwork of homogeneous material giving the staining reactions of fibrin, and a zone of cellular proliferation, in which the characteristic cell is large and of a fibroblastic type. The nodules are microscopic in size, and vary in shape according to their surroundings. The emigration of leukocytes is moderate and diffuse, mononuclear types predominating. There are comparatively slight degenerative and necrotic changes.

These nodules are found in all three layers of the heart, but all three layers are not always involved in the same case. Very rarely are the lesions confined to a single layer, at least two being usually affected. The myocardium is involved most frequently, in children at any rate, with the endocardium next. In the myocardium the nodules are closely related to the coronary arterioles. In the endocardium they are seen in the deeper parts of the valves. The proliferation and degeneration of the surface endothelium over the nodules and the deposit of fibrin on the denuded surface, and the subsequent formation of new connective tissue, forms the well-known vegetations, and leads to the subsequent valvular deformity. In the pericardium the nodules lie under the endothelium, in which the same changes occur, leading to the recognized lesions of rheumatic pericarditis. It is in these nodules that the organisms are mainly found, and this I believe explains the negative bacteriological results ob-

tained by so many investigators. The distribution of the nodules suggests that the organisms reach the heart valves, not by being deposited by the blood flowing through the cardiac chambers, but by the coronary arteries.

SYMPTOMS. THE ONSET.—As to the mode of onset of rheumatic fever, we find that in the adult the disease begins almost invariably with fever and arthritis, usually polyarthritis, characterized by pain, tenderness, redness, and swelling of the affected joints. In an analysis of 223 cases of rheumatic fever in children, I found that the mode of onset was as follows:

TABLE 58

Mode of Onset in Rheumatic Fever

	CASES
Fever and arthritic symptoms.....	88
Fever and cardiac symptoms.....	82
Fever and both arthritic and cardiac symptoms.....	25
Fever only.....	18
Fever and sore throat.....	6
Fever and chorea.....	1
Unknown.....	3

From this it appears that, although a little the most common mode of onset is with symptoms referable to the joints alone, an onset with symptoms referable to the heart alone is almost as common. By cardiac symptoms are meant not the evidence of insidiously developing endocarditis disclosed by the detection of a murmur, but actual symptoms of cardiac weakness, such as precordial pain, dyspnea, and orthopnea. It is also notable that, although the onset with arthritic symptoms alone is commoner than any other one mode of onset, yet it existed in only 40 per cent of all the cases. The number of cases in which the disease manifested itself at the onset by the occurrence of fever only, with or without slight and vague constitutional symptoms, is of special interest in connection with the practical question of diagnosis. It shows that rheumatic fever in children must be placed in that class of acute infectious diseases which do not necessarily show characteristic or localizing symptoms at the onset, and in which the diagnosis must often be for several days in doubt, until such symptoms have developed. When, as so often happens, the physician is confronted with a beginning acute infectious disease, in which the physical examination and history are not illuminating, he must not forget to number rheumatic fever among his possibilities. The onset with sore throat as the only symptom accompanying the fever in six cases, is also of interest. In consideration of the fact that children only complain of sore throat in a small proportion of cases in which inflammation of the pharynx or tonsils is found on physical examination, it is very possible that

the number of cases in which such inflammation was actually a symptom of onset might have been larger if proper observation could have been employed.

THE FEVER.—The temperature curve of rheumatic fever, while showing the widest variations in different cases, both as to the degree of temperature attained and as to its duration, nevertheless presents certain features which I believe are fairly characteristic of this disease. The amount of fever varies with the severity of the case and with the localization of the infectious process, every gradation being found from the most moderate fever curve, ranging between 99° and 100° , to one reaching 105° or even 106° . Hyperpyrexia, however, is rare in children, being very much less common than in adults; in an average case in a child the fever ranges between 101° and 103° at the height of the disease. The temperature is higher in the cases with cardiac symptoms than in those with arthritic symptoms only, and, in general, higher in cases of pericarditis than in cases of endocarditis. The most notable characteristic of the temperature curve in rheumatic fever is the absence of any very wide daily variation in the temperature, the variation being, in the majority of cases, about one degree, and not often over two degrees; the morning temperature is almost always the lower. There are, of course, marked exceptions to this rule to be encountered at times; nevertheless, sudden exacerbations, remissions, or critical falls in the temperature are uncommon. The temperature usually rises rapidly, but not with extreme suddenness, and in most of the arthritic cases and the milder cardiac cases falls rapidly, but not suddenly, to the normal. The maximum is by no means always reached near the beginning of the disease, as at any time a further exacerbation may occur, in which the fever increases fairly rapidly, but again not suddenly. The course of the fever may be prolonged over a period of weeks or months with frequent exacerbations, especially in the cardiac cases, the longest fevers being found in cases of pericarditis. In such cases the termination is by a much less rapid lysis than in the arthritic and milder cardiac types. The duration of fever in 223 cases was as follows:

	AVERAGE	EXTREME
In cases with arthritic symptoms only.....	4 days	1 day to 2 weeks
In cases with endocarditis.....	12 days	1 day to 12 weeks
In cases with pericarditis.....	39 days	2 days to 12 weeks

In comparison with adults, the shorter duration of the fever in the articular cases, and the frequent exceedingly long duration of fever in the cardiac cases, form a very characteristic feature.

CONSTITUTIONAL SYMPTOMS.—These, while sometimes present, are usually absent or slight in children. In some cases the fever of onset is accompanied by some headache and vague aching pains in

the back and limbs, without pain on motion or tenderness in the joints. Such cases are frequently diagnosticated as gripe. There are almost never general symptoms referable to the nervous system. The profuse acid sweating, so commonly seen in adults, is comparatively uncommon in children, especially during the earlier years of childhood.

ARTICULAR MANIFESTATIONS.—The joint symptoms of rheumatic fever in children deserve detailed mention. The first peculiarity of the disease which struck my attention in analyzing a series of cases, was the comparative infrequency of joint symptoms in children suffering from an acute infection which other evidences pointed to as being rheumatic fever. Out of 223 consecutive cases admitted to the Children's Hospital suffering from rheumatic fever, only 102 (45 per cent) had joint symptoms. A second point is their great mildness in comparison with rheumatic fever in adults. Not only are the objective manifestations of swelling, redness, and heat comparatively infrequent, but the pain on motion is much less severe, often being so little as to cause only a slight limp, and the tenderness to pressure is often but slightly marked, or absent. Redness and swelling were present in only about 50 per cent of the cases having joint symptoms, and in only 20 per cent of all the cases of rheumatic fever in the series. The duration of the joint symptoms in children is also very brief, averaging a little less than two days.

This frequent great mildness and extremely short duration of the arthritic symptoms, combined as they so often are, with very slight fever and no constitutional symptoms, account for the fact that rheumatic fever in children is so frequently overlooked. The symptoms, even when complained of by the child, are often attributed by the parent to "growing pains," and in other cases, in which the only manifestation is a slight limp in walking or complaint on using a limb, the disability is attributed to a strain.

As to the number of joints affected in children, there is wide variation. Only one joint may be affected, and the process is confined to one joint more often in children than in adults (10 per cent of my series). Usually more than one joint is affected, but the number is in general fewer than in adults, a general polyarthritis being rare. The ankles are the joints most frequently affected, the knees being second and the wrists and hands third.

In this description of the arthritic manifestations of rheumatic fever I have laid stress on the general and typical peculiarities in children, but I do not wish to convey the impression that the disease never occurs in childhood in the same severe arthritic form as in adults. Cases are seen in which there is high fever, polyarthritis, with extreme pain on motion, tenderness, redness, and swelling, and in which

there are even profuse acid sweats. Such cases are, however, not typical, and occur most often in older children. Indeed, a striking feature in the rheumatic fever of early life is the variation of its manifestations according to age. The younger the child, the more apt are the peculiarities mentioned above to be accentuated, arthritic manifestations being slight and cardiac manifestations prominent. The nearer adult life is approached, the more does the type of disease approach that seen in adults.

CARDIAC MANIFESTATIONS.—The cardiac manifestations of rheumatic fever in children are of importance, in the first place on account of their great frequency of occurrence. In my series, 91 per cent of all cases had evidence of an organic lesion in the heart, which is a very much larger proportion than that observed in the rheumatic fever of adults. The commonest clinical form is endocarditis, found

FIG. 153



Rheumatic fever. Adult type of disease. Male, $3\frac{1}{2}$ years old

in 91 per cent, pericarditis occurring in 26 per cent. It is, however, not so much this frequency of occurrence of cardiac involvement which constitutes the most important peculiarity of rheumatic fever in children, as it is the effect which acute endocarditis has upon the symptomatology of the disease. In the adult, endocarditis is usually described as developing insidiously, betraying itself only by the appearance of a murmur. In children, endocarditis usually betrays itself by the occurrence of actual symptoms referable to the heart. Its occurrence may be insidious, as in the adult, but in very few of my cases did a murmur actually develop unaccompanied by cardiac symptoms. There were cases in which a murmur was found without symptoms, but in such cases it was not possible to know if acute endocarditis was actually present, or if the murmur was the relic of some previous attack. In 65 per cent of my cases having a murmur

there were actual cardiac symptoms. These symptoms themselves are the ordinary ones of cardiac weakness:—dyspnea, palpitation and precordial pain in the milder cases, with the addition of edema and cyanosis in the severer ones. *The symptoms are not due to mechanical interference with the circulation because of the valvular lesion, but to the myocarditis which usually accompanies the endocarditis, and which is the most common of the rheumatic cardiac lesions in early life.* The term “broken compensation,” so often used in describing cardiac symptoms in adults, is not applicable to the symptoms seen in the course of an acute attack of rheumatic fever in childhood, because the term implies that the cause of the symptoms is the overtaking of a damaged but “compensated” heart. In children the cause of the symptoms is not such overstraining of a compensated heart, but rather an acute infection of the myocardium.

The valvular lesions show no important peculiarities, and are of comparatively little clinical significance. The mitral valve is by far the one most frequently affected. Pericarditis in children shows no special peculiarities in symptomatology. The majority of cases go on to effusion. It is not the character of the cardiac symptoms which is of importance, but their severity, obstinate duration, and danger to life. They are accompanied by fever and evidence of acute infection, and I believe the frequency of death from heart disease in children is not due to the overstraining of chronically damaged valves, but to the liability of children to acute rheumatic infection of the heart, causing myocardial weakness.

The cardiac symptoms of rheumatic fever in early life may precede, accompany, or follow arthritic manifestations.

A very important peculiarity of rheumatic fever in children lies in the occurrence of cases in which the only localization of the infection is the cardiac—the *primary acute rheumatic endocarditis of childhood*—cases which run a course characterized by fever and cardiac symptoms only.

RECURRENCES.—Finally must be mentioned one of the most important peculiarities of rheumatic fever in childhood, *the liability to recurrence of the infection with varying manifestations.* It is not uncommon for these recurrences completely to dominate childhood. There is no special order for the various clinical types to appear, and each attack may be mild or severe. At one time the symptoms are mainly cardiac, at other times mainly articular, at still other times a combination of both types. Any attack may be accompanied by pericarditis or followed, accompanied, or even preceded by chorea. In any attack the severity of the cardiac symptoms may lead to a fatal ending.

OCCASIONAL MANIFESTATIONS.—Next to the lesions of the heart

and joints, the most constant clinical manifestation of rheumatic fever in early life is *anemia*. The rheumatic fever poison appears to have a particularly marked effect upon the blood, and the anemia produced is often extreme. The chief peculiarity of the anemia symptomatic of rheumatic fever is the *great rapidity* with which it develops.

Chorea must be regarded as a manifestation of the rheumatic fever infection rather than as a separate etiological entity of which rheumatic fever is a contributing cause. The evidence in favor of the connection between chorea and rheumatic fever is not only clinical, but bacteriological. The frequent occurrence of chorea during or after an attack of rheumatic fever has long been known. In some animal experiments carried on with rheumatic fever organisms, choreic movements have been observed. Rosenow obtained symptoms of meningeal irritation and localized nodular areas in the pia mater with certain strains of streptococci derived from rheumatic fever patients. Finally, the important work of Dick and Rothstein has conclusively shown that chorea is due to a streptococcus having peculiar properties.

Why chorea is only seen in some cases, is not definitely known. The probability that the rheumatic fever streptococcus includes a number of strains with varying virulence and affinities, is the most plausible explanation of this phenomenon. It is also impossible at present to state with certainty that all cases of chorea are instances of streptococcus infection. In my chorea cases, over 60 per cent were children showing at some time other rheumatic fever manifestations.

Chorea may be the first manifestation of infection in any attack, to be followed later by articular or cardiac symptoms. It may occur simultaneously with the symptoms, may follow them, or may be the only manifestation in any single attack.

Tonsillitis stands next in frequency to chorea as an occasional manifestation of rheumatic fever. It is certainly true that not all cases of tonsillitis, nor even the majority of cases, are caused by the rheumatic fever type of streptococcus. Nevertheless tonsillitis so frequently precedes or ushers in an attack of rheumatic fever, that the clinical connection in many cases cannot be doubted. Furthermore, the rheumatic fever type of streptococcus has been found in the throat in tonsillitis. We can only conclude that while tonsillitis is due to a variety of infections, rheumatic fever is one of them, and in this sense tonsillitis must be considered one of the manifestations of the disease.

Torticollis is the most frequent form of myositis which occurs in the rheumatic fever of early life. Not all cases of torticollis are due to this infection, but in some cases the connection is certain. These

cases are characterized by the sudden development of tonic spasm of the sterno-cleido-mastoid, by marked tenderness and pain on motion, and by the fact that the spasm disappears spontaneously within a few days. Other forms of myositis are less common, and usually affect the muscles of the extremities.

Pleurisy, usually dry, characterized by pain on breathing and coughing, and by the appearance of a pleuritic friction rub, is seen at times, especially in prolonged cases with cardiac manifestations. Peritonitis is very rare.

The Subcutaneous Nodules found at times in cases of rheumatic fever are undoubtedly a specific manifestation of the disease. Their microscopic anatomy is very similar to that of the submiliary nodules of the heart, although they are much larger. They were described first by Barlow and Warner, as "oval, semi-transparent, fibrous bodies like boiled sago grains." These nodules vary in size from that of a large pin's head to that of a small bean, or larger. They come in crops, and may last only a few weeks and then disappear, or may persist longer. They are found most frequently at the back of the elbows, at the sides of the ankles, and above the patellae, but may occur on the backs of the feet and hands, along the spine, and in other parts of the skin. They can be seen when the skin is tightly drawn, but are more easily detected by palpation.

When present, these subcutaneous nodules are diagnostic of rheumatic fever. Judging by published reports I should say that they are seen much more commonly in England than in this country, and probably also more often in some parts of this country than in others. They are rarely seen around Boston.

There is also an undoubted connection between certain forms of erythema, of which *erythema nodosum* is the type, and rheumatic fever. It has not, however, been established that rheumatic fever infection is the sole cause of these lesions. Both *erythema multiforme* and *purpura* are frequently associated with rheumatic fever. These conditions, however, are known to be symptomatic of a number of diseased conditions, rheumatic fever being among the number, and they cannot be considered as specific manifestations of the latter disease.

SUMMARY OF THE CLINICAL TYPES OF RHEUMATIC FEVER.—It is difficult to divide a disease with such varied and changing symptoms into distinct clinical types. The following division is based upon the character of the onset and the severity of the case; it must be remembered that at any time in an articular type of case cardiac symptoms may develop, and vice versa, and that even the mildest cases after recovery usually are left with a permanently damaged heart:

1. The mild arthritic type. These are cases with slight and brief fever and joint symptoms only, of a mild and brief, even fleeting character, confined to one or few joints.

2. The severe arthritic type. This occurs in older children, with a severe polyarthritis resembling the adult type.

3. Latent type. In these cases there is at the onset a period with fever as the only symptom. Later may occur cardiac or arthritic symptoms, which may be so mild as to escape notice, or which may at any time become severe.

4. Mild primary endocarditis. These cases are characterized by fever, and slight dyspnea, palpitation or precordial pain, the symptoms being of brief duration. Slight joint symptoms may develop in the course of the disease.

5. Severe primary endocarditis. These cases are characterized by fever and the whole train of the symptoms of cardiac incompetency. They usually run a prolonged and obstinate course, recovery occurring very gradually. At times death occurs from failure of the heart.

6. Mild pericarditis. In these cases precordial pain is the most prominent symptom, accompanied by fever and the other signs of cardiac weakness. They usually run a fairly long course. Effusion may or may not occur, and, a notable point, it may occur without increase in the severity of the cardiac symptoms. Cases of pericarditis almost invariably show endocardial murmurs also.

7. Severe pericarditis. In this type, the fever is high, long continued, and obstinate, and precordial pain is severe at the onset. Effusion always occurs. The symptoms of cardiac insufficiency become very marked, and their severity usually shows little relation to the amount of effusion, although at times a sudden increase in their severity occurs in parallel with a sudden increase in the extent of the effusion. Recovery is slow, and death, when it occurs, is due to cardiac weakness.

DIAGNOSIS.—The successful diagnosis of rheumatic fever in childhood depends upon thorough familiarity with the peculiarities of the disease in early life. The physician must free his mind from all preconceived notions of "acute articular rheumatism" drawn from the manifestations of the disease in adults.

The disease presents itself for diagnosis usually in one of three clinical forms: (1) Fever with pain in the joints or limbs on motion; (2) fever and cardiac symptoms; (3) fever without definite symptoms.

The family history may have some bearing on the diagnosis, as heredity is one of the etiological factors. The previous history is extremely important. The evidence points strongly toward rheumatic fever if there is a previous history of any of the following mani-

festations: Joint symptoms no matter how slight, even if they be only indefinite pains in damp weather, or growing pains; any cardiac symptoms; chorea; frequent attacks of tonsillitis; any of the other manifestations of rheumatic fever. The importance of the previous history is due to the tendency of the disease toward recurrences. The physical examination is also of the greatest importance. The signs to be looked for are signs of endocarditis or pericarditis, signs of arthritis, anemia with a history of rapid development, and subcutaneous nodules.

On the other hand, if the patient is under the age of five years the probability of rheumatic fever is greatly lessened, and if under two years, the probabilities are strongly against the disease.

The combination of pains in the joints on motion and fever with sudden onset, usually means rheumatic fever, unless some other cause, such as another recognized acute infection, can be found. If there is redness, swelling, and tenderness to pressure, the diagnosis is strengthened, but these signs are usually absent in the younger children. If more than one joint be affected, this also strengthens the diagnosis of rheumatic fever, but it must be remembered that monarticular involvement is not uncommon in early life. If there is evidence of a cardiac lesion, the diagnosis is almost certain.

The cases which present the clinical picture of fever and cardiac symptoms are much easier of diagnosis. When in such cases the physical examination shows signs of a cardiac lesion, and when there is no evidence of any other recognized infectious disease, such as diphtheria or scarlet fever, the diagnosis is practically certain. Nevertheless such cases are often diagnosed as chronic endocarditis with "broken compensation," especially if there has been a previous attack leaving a chronic valvular lesion. The occurrence of a fresh attack of rheumatic fever is overlooked, because the physician regards endocarditis as a complication of arthritis, and associates a fresh attack with fresh articular symptoms. The commonest cause of cardiac symptoms in childhood is a fresh infection localized in the heart, and when such symptoms are accompanied by fever, this diagnosis is almost certain.

The type characterized by fever without definite localizing symptoms is the most difficult of diagnosis. The diagnosis is usually impossible until a murmur develops in the heart, or until arthritic or cardiac symptoms appear. I have often seen such cases diagnosed as gripe. It is important to recognize the possibility of rheumatic fever in any acute infection with indefinite manifestations. When there is a previous history of any rheumatic fever manifestations, the disease should be strongly suspected even before definite symptoms appear.

Rheumatic fever is more frequently overlooked than confounded

with other diseases. The conditions most frequently mistaken for rheumatic fever are multiple neuritis, syphilitic bone disease, tuberculosis of the bones and joints, scurvy, acute osteomyelitis, and multiple secondary arthritis.

Multiple neuritis is recognized by the extreme tenderness along the course of the nerves. Syphilitic bone disease is much more chronic, and the involvement of the bone or periosteum is usually clearly apparent. Tuberculosis is also more chronic, but the diagnosis is often difficult, the deciding factor being often the presence or absence of cardiac involvement. Scurvy is only seen in the first two years of life, a period when rheumatic fever is extremely rare, and the lesion is definitely associated with the bones. In osteomyelitis the epiphysis or shaft of the bone is involved rather than the joint, the localized symptoms are more intense, and the constitutional symptoms usually more marked. Multiple secondary arthritis is diagnosed through the recognition of the primary infection, but gonococcus arthritis is often diagnosed as rheumatic fever. I have even seen cases of epidemic meningitis with pronounced pain on motion of the limbs, diagnosed as rheumatic fever, through overlooking of the meningeal symptoms.

PROGNOSIS.—The prognosis and mortality of rheumatic fever as given in many text books is based on the articular manifestations alone, the cardiac manifestations being considered complications. This is not a proper way of estimating the seriousness of the disease in childhood. If all the manifestations and peculiarities of the infection in early life are taken into consideration, rheumatic fever appears as a very serious disease. There are three causes for the especial seriousness of the disease in childhood. These are, first, the great liability of children to be attacked by rheumatic fever; second, the great liability of children to recurrence; third, the great liability of children to cardiac involvement.

In considering the prognosis in any given case, we must consider first the immediate prognosis, that is, the chances of recovery from the particular attack, and second the ultimate prognosis, that is, the chances of ultimate survival, with or without permanent cardiac disability.

IMMEDIATE PROGNOSIS.—The outlook for recovery in any attack of rheumatic fever depends first upon whether there is evidence of cardiac involvement. If the process is confined to the joints, and if no cardiac signs or symptoms develop, the outlook is wholly favorable. When the heart is involved, the immediate prognosis depends on the severity of the cardiac symptoms. If the only sign of cardiac involvement is the presence of an organic murmur, the outlook is favorable. When signs of cardiac weakness are present or develop,

the immediate prognosis becomes more doubtful, and depends upon the severity of the cardiac disturbance. The physician must remember that the signs of weakness of the heart are not due to relative over-exertion, but to an acute infection of the heart, and therefore treatment with rest and digitalis cannot touch the cause. The progress of the infection is very difficult to predict. If there is only precordial pain, palpitation, and moderate dyspnea, the outlook is fairly good. If there is severe dyspnea, marked dilatation, edema, or signs of pericarditis, the outlook is very doubtful. A great many children die in the acute stage of rheumatic fever involving the heart, and the most common cause of death from cardiac failure in childhood is not broken compensation, but rheumatic fever infection.

In my series of cases, the immediate mortality of 209 cases in which the rheumatic fever infection affected the heart, was as high as 20 per cent. This of course was hospital mortality, and is perhaps slightly higher than it would be outside. Nevertheless, when one remembers that the heart is involved in 90 per cent of all cases of rheumatic fever in childhood, and that the immediate mortality of these cases may be as high as 20 per cent, one begins to realize the seriousness of the disease in childhood.

ULTIMATE PROGNOSIS.—What is the outlook for a child who survives his first attack of rheumatic fever? During the remaining years of childhood such a patient is constantly in danger on account of the tendency of the disease to recur one or more times. In my series there was more than one attack in 76 per cent. In each of these subsequent attacks, the disease may assume a severe type and prove fatal. In a series of 180 cases followed till they were fourteen years old, 85 died subsequently, a mortality of 47 per cent. The cause of death in most of these cases was a fresh acute infection, although a few died from broken compensation.

After adult life is reached, the outlook is entirely different. The cases in my series which entered adult life with damaged hearts were ninety-five in number, and of these only seven died in the next ten years, a mortality of a little over 7 per cent. Here we come to a more favorable side of the picture. Not only is the mortality low in children who enter adult life with hearts damaged by rheumatic fever, but the disability caused by such damaged hearts is surprisingly slight. The danger of cardiac disability, attacks of broken compensation and so forth, in adults who acquired their cardiac lesion in childhood, is much less than in adults who acquired it in adult life. This will be further discussed in the Division on Diseases of the Heart.

To summarize the prognosis of rheumatic fever, one would say that it is a dangerous disease in childhood, with constant danger from recurrence and cardiac failure. If, however, the child escapes

the dangers during childhood, the outlook for a useful adult life without cardiac disability is good.

PROPHYLAXIS.—Before the occurrence of the first attack of rheumatic fever, there is nothing which can be done in prophylaxis beyond the general measures of hygiene which insure the best development of the normal child. I am not an advocate of removing the tonsils from all children merely as a prophylactic measure against rheumatic fever. If, however, a child is subject to frequent attacks of tonsillitis, the tonsils should be removed.

After a child has recovered from its first attack of rheumatic fever, I believe that removal of the tonsils is positively indicated in every case. The hygienic surroundings should be carefully investigated, and every unfavorable feature remedied. If a second attack occurs, I recommend a change of climate whenever it can be managed. Such a patient should always spend the winter and spring in a warm dry climate. There is probably no relation between the diet and rheumatic fever, and no special modifications should be made in the diet of children subject to the disease. The idea that they should not eat red meat is based on wholly faulty reasoning. The diet should be that of the normal child of that age, care being taken to avoid indiscretions.

Rheumatic fever patients between attacks should always be protected from sudden changes of temperature. In winter extra care must be taken not to allow them to become exposed to unfavorable weather conditions. Woolen underclothing should be worn the entire year, the very lightest weight being used in summer.

TREATMENT.—Whenever a child complains of any pain in the limbs, it should at once be confined to the house in a warm room. The temperature should be carefully watched. Any rise of temperature under these circumstances should be the signal for at once confining the child to bed.

When the diagnosis is made, the child should be *kept in bed as long as there is any fever or cardiac symptoms*. It should wear a flannel nightgown, and the room should be kept at an equable temperature. The diet should be that of any acute febrile disease, consisting chiefly of milk, cereals, soups, and broths, the only limitations being those of the child's digestion.

Two forms of drug treatment have been widely recommended as having an especially favorable influence in rheumatic fever, the *alkalies* and the *salicylates*.

The alkaline treatment is based on the fact that in rheumatic fever the urine and sweat are highly acid. There has never been any definite evidence that the alkalies have any influence on the cause or course of the disease. Nevertheless it is quite probable

that the rheumatic fever streptococci produce acids, and indeed Rosenow has found marked acid production in his cultures. The giving of alkalis is therefore legitimate symptomatic treatment. The acetate or citrate of potassium or the bicarbonate of sodium may be used in doses proportioned to the age of the child. The object is to make the urine alkaline, and the amount of alkali given must be increased if the desired effect is not obtained.

There is no doubt that the *salicylates* have a specific action in controlling the symptom of pain in rheumatic fever, whether the pain be referred to the joints, to the heart, or to the muscles. The question as to whether the salicylates are etiotropic, that is, whether they act upon the specific cause of the disease in such a way as to hasten recovery, is one about which much difference of opinion exists. Many authorities believe that the salicylates have such action, and many articles are written advocating the superior value of one or another of the various forms of salicylate. The evidence on which these conclusions are based is all of the unsatisfactory, purely clinical variety. No other infectious disease caused by a bacterium has yet been found to be specifically influenced by any drug, and the specific action of the salicylates in rheumatic fever is contrary to all analogy. Even the supporters of this view qualify their statements by admitting that salicylate therapy does not have much action in hastening recovery from cardiac involvement. The chief evidences of the value of the salicylates in apparently hastening recovery have been obtained in the severe polyarthritis of adults. We must admit that the question is still an open one.

Insofar as children are concerned, the joint manifestations tend to disappear rapidly, and the cardiac manifestations to persist obstinately. I do not believe that continued use of any form of salicylate will hasten the recovery in cardiac cases. Consequently, I believe that *in children the salicylates should be used mainly in the symptomatic treatment of pain*, although there is no objection to giving small doses for a longer period provided that they do not disturb the stomach. My preference is for the *sodium salicylate* as a routine, given in doses proportioned to the age of the child as shown in Division II. If salicylate of soda is ineffective or disturbs the stomach, *aspirin* should be substituted. Other substitutes to be tried in troublesome cases are oil of wintergreen, salicin, salol, and salecetin.

The articular symptoms of rheumatic fever in childhood rarely require further treatment than the salicylates. In very severe cases resembling the adult type, protection of the limb from the weight of the bedclothes, and hot fomentations to the joints, should be employed as in adults.

The treatment of the cardiac symptoms of rheumatic fever will be more fully described under diseases of the heart. The essential

thing in treatment is to keep the child absolutely quiet in bed until all symptoms have disappeared. During the acute febrile stage of the disease, *digitalis and other cardiac stimulants should not be employed*, except as a last resort in threatening cardiac failure. The process is an acute infection of the heart, and stimulation appears only to aggravate the process. If the child is very restless, bromides, and sometimes even opiates may be employed. An ice bag applied to the precordia is very useful.

The management of convalescence depends entirely upon the condition of the heart, and will be described under that organ. If the heart is not involved, convalescence is managed as in any acute infection. The anemia must be combatted with iron, and cod liver oil is a useful tonic.

PROBLEMS AND RESEARCH.—The chief problem which is occupying the scientific research workers on rheumatic fever, is that of etiology. There have been three principal theories as to the cause of the disease.

The first theory is that rheumatic fever is not an infection. There have been various theories as to a chemical (acid), nervous, or thermal etiology. Some authorities, while refusing to accept these theories, have believed that the disease was due to some virus wholly different from the ordinary forms of bacteria. A second view regarded rheumatic fever as a particular reaction of the tissues to a number of different varieties of bacteria. Under this view the lesions in the joints and heart are produced not necessarily by the presence of bacteria themselves, but possibly by the absorption of their toxins from some distant focus. Sahli was one of the original expounders of this view; he regarded rheumatic fever as due to microorganisms of low virulence,—attenuated streptococci or staphylococci. The expounders of this theory have never been very clear in their explanation of why a variety of organisms should produce so constant and peculiar a tissue reaction. The third view regards rheumatic fever as due to some *specific form of bacterium*.

The principal evidence against the infectious nature of rheumatic fever was wholly negative in character, and consisted in the failure of many thoroughly skilled investigators to isolate any bacteria from the lesions which could be definitely associated with the disease. Against this negative evidence was the classical work of Poynton and Paine in England, who recovered a diplococcus from a large percentage of their rheumatic fever patients, and were able to reproduce in rabbits and other animals every phase of rheumatic fever including the cardiac lesions, recovering the same organism from these lesions. Many observers in all parts of the world have reproduced these experiments with identical results.

Nevertheless the diplococcus rheumaticus was not generally accepted as the specific cause of rheumatic fever, particularly in this country, where the observers who obtained negative cultures were in the majority. It was a known fact that many varieties of infection are attended by articular and cardiac complications, and this was used as an argument against the specific etiology of rheumatic fever. It was shown experimentally that streptococci in general have a certain affinity for the joints, and that both arthritis and endocarditis could be produced with strains of streptococci obtained from sources other than rheumatic fever lesions, and this was advanced in favor of the second view outlined above, that rheumatic fever is a specific tissue reaction against various forms of infection, streptococcus infection in particular. Nevertheless this work really favored the specific etiology of rheumatic fever, because the lesions produced by various forms of streptococci were not constant in character, and differed markedly from the lesions produced by organisms isolated from rheumatic fever patients, and those obtained with the diplococcus rheumaticus. The differences correspond quite closely to the differences observed clinically in rheumatic fever on the one hand, and streptococcus arthritis on the other.

The principal objection, beside the negative findings of many skilled observers, to the acceptance of a specific organism as the cause of rheumatic fever, was the fact that there were at first no important morphological or cultural characteristics which served to distinguish the "diplococcus rheumaticus" from other varieties of streptococci. Continued study of the streptococcus group, however, has recently been attended by marked progress in separating the various strains of streptococci one from another.

The work of Rosenow is the most important contribution to the subject of streptococcus infection in general, and rheumatic fever in particular, which has yet appeared. He found that changes in oxygen pressure exercised an important influence on the growth of microorganisms of the streptococcus group. On the basis of gradations of oxygen pressure he devised a technique by which he got pure cultures from the joint fluid in sixteen out of nineteen non-fatal cases of rheumatic fever, and from the blood in five out of eight cases.

The strains of streptococci obtained in this way all differed in one respect or another from ordinary strains of pus-producing streptococci, and from the *streptococcus viridans*. When injected into animals they did not produce pus, and exhibited an affinity for the endocardium, pericardium, and synovial membranes. Rosenow further observed a tendency of these various strains of streptococci to *localize in experimental animals at sites corresponding roughly to the sites of the lesions in human cases whence they were obtained*. Thus strains from myositic lesions in man caused myositis and myocarditis

in animals, whereas strains from human cases without myositis caused arthritis and endocarditis only in animals. This observation is very suggestive in connection with the peculiar selective affinities observed in rheumatic fever infection.

The part of Rosenow's work which is most suggestive of the progress to be made in the future, is his experiments on the *transmutation* of bacteria. Working with the streptococcus group of organisms, he has been able by animal passage and by other means to convert one type into another. Thus he has been able to convert typical hemolytic streptococci into pneumococci and vice versa. He believes that he can convert the rheumatic fever streptococci into other members of the group, as for instance, into the *streptococcus hemolyticus* on the one hand, and the *streptococcus viridans*, or some variety of the *pneumococcus*, on the other.

This work, if it be confirmed, will revolutionize our views of streptococcus and pneumococcus infection. Instead of regarding the various members of the general group, *pneumococcus*, *streptococcus hemolyticus*, *diplococcus rheumaticus*, *streptococcus viridans*, as distinct strains having constant pathogenic properties, we must regard them as one great variety which under various conditions may be altered in its virulence and pathogenic properties. If streptococci may undergo such changes outside the body, when grown in symbiosis with other bacteria or under varying degrees of oxygen pressure, they may similarly acquire new properties within the body, in the tonsils, for instance, where, as suggested by Rosenow, conditions are favorable. Thus each manifestation of streptococcus infection would depend upon the type of streptococcus which had been produced by the conditions under which the organism had been existing.

The question of a specific therapy with serum or vaccine in rheumatic fever must await the results of further work along the lines indicated above. The organism which causes the disease has been too recently discovered and too insufficiently studied as yet to afford a firm basis for immune treatment. It is highly probable if not certainly proven that the various strains of the streptococcus group produce each a specific immune reaction in the human body. It is probable also that the type of streptococcus which produces rheumatic fever itself includes several strains. Consequently the outlook for a serum therapy is at present not very encouraging. For an effective vaccine therapy the prospects are somewhat brighter. Obviously, if there are different strains with specific immune reactions, stock vaccines are not likely to be successful. With the improvement in bacteriological technique—improved methods of isolating the organisms from the body of the patient—the possibility of using autogenous vaccines is not very remote. The prolonged course of the cardiac infection in children suggests that this form of the dis-



ease may eventually prove amenable to vaccine treatment. Still greater is the possibility of the successful use of vaccines in preventing the dangerous recurrences of the disease.

ERYSIPELAS

Erysipelas is an acute infectious disease, characterized by an inflammation of the skin, spreading through the lymphatics.

ETIOLOGY. THE MICROÖRGANISM.—The cause of erysipelas is the *streptococcus vulgaris hemolyticus* (common *streptococcus pyogenes*). This organism is the most common type of pus-producing streptococcus, and is found in most cases of general streptococcus septicemia, in many localized purulent inflammations, and in certain other localized inflammatory lesions. There is no known means of distinguishing the streptococcus which produces erysipelas from the streptococci associated with these various pathological processes. Consequently erysipelas cannot be considered a specific infectious disease, and under a strict classification should be described under the diseases of the skin. Nevertheless the pathological anatomy and clinical manifestations of erysipelas are so peculiarly characteristic, and so much like those of a specific infection with general constitutional symptoms, that the disease can be most conveniently and strikingly described in connection with the specific infections. Also, the most recent research has raised the question whether the streptococcus group of organisms cannot be further subdivided upon a basis of acquired selective affinity for certain tissues and organs. It is possible that erysipelas may be due to a strain of *streptococcus hemolyticus* which has acquired properties which cause it to produce the peculiar lesions of the disease. For these reasons I have felt justified in departing from a strict basis of classification in order to describe erysipelas in this Division.

MODE OF INFECTION.—The streptococcus enters through some lesion of the skin or mucous membrane. In the newborn the usual portal of entry is the umbilicus. In later infancy the portal of entry is usually some small lesion of the skin, particularly on the face, such as might be produced by a scratch, insect bite, a patch of eczema, an excoriation or fissure about the nose, lips, or ears. In older children the most common portal of entry is the mucous membrane of the nose, which has become excoriated from rhinitis or trauma. At all ages erysipelas may follow the infection of a wound or an ulcer. Formerly infection through vaccination or circumcision was fairly common, but with modern precautions it is extremely rare.

The streptococcus is an organism of such wide distribution, that direct transmission from one case to another plays practically no part. Formerly, before the days of asepsis, when conditions of un-

cleanliness prevailed in hospitals, erysipelas was a common complication of surgical procedures, and direct transmission played a more important rôle. Today, instances are extremely rare. The disease usually occurs through autoinfection. Streptococci are constantly present in the nose and mouth, and upon an unclean skin, and these organisms, through unknown conditions, may acquire the virulence required for the production of the disease.

PREDISPOSITION.—Erysipelas is commoner in infancy than in later childhood, but even in infancy is less common than in adult life. The more common occurrence of the disease in infancy than in childhood is to be accounted for by the very great frequency in infants of excoriations and other lesions of the skin and mucous membranes. When one considers the frequency of such lesions in the first two years of life, it is surprising that erysipelas is not more common, as both conditions necessary for infection, the streptococcus and the portal of entry, are present. One is forced to conclude that there is less susceptibility to the disease in early life than in adult life. This lessened susceptibility is probably due not to a general relative constitutional immunity, but to the fact that the lymphatic apparatus of the skin in early life is more resistant to the spread of streptococcus infection.

Lowered constitutional resistance probably plays a part in individual cases of erysipelas.

IMMUNITY—Erysipelas is a self-limited disease, and often terminates by crisis. The course of the disease is, however, very variable and erratic, and the immunity conferred by an attack cannot last long, as recurrences are not uncommon.

PATHOLOGICAL ANATOMY.—The deeper layers of the skin are swollen by an accumulation of serous fluid, which may be nearly transparent, or turbid from admixture with pus-cells. The pus-cells may infiltrate the tissues either sparsely or in dense masses. Sometimes vesicles are found on the surface, or there may be crusts. At times more or less of the affected region is filled with abscesses or becomes gangrenous. In other cases, aside from the local lesions, petechiae are found in the serous membranes, and there may be swelling of the spleen and parenchymatous degeneration of the kidneys and liver. When the mucous membranes are affected they show the same appearances as the lesions of the skin, except so far as these are modified by the different structure of the tissue. The disease may attack the larynx and upper air-passages and result in edema. Pneumonia may occur as a complication.

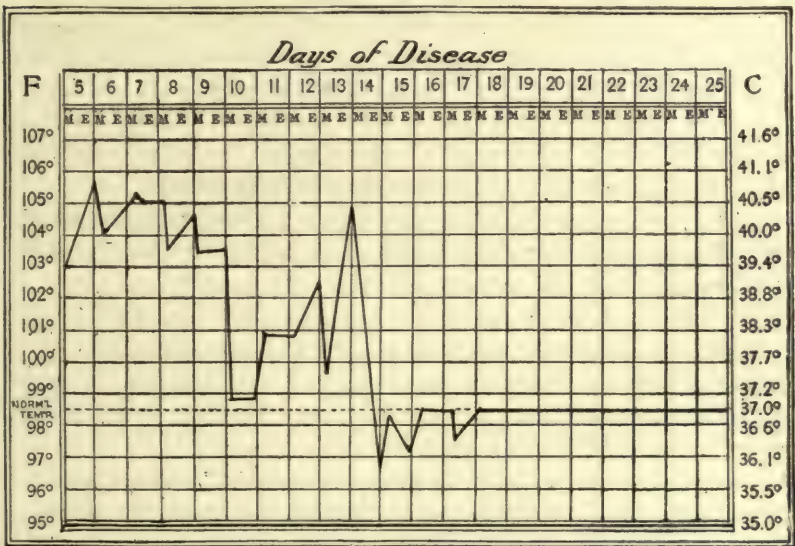
Although the different organs, such as the spleen, kidney, heart, and liver, at times show pathological changes, nothing characteristic

of erysipelas has been found in these organs, but only such changes as may occur from a continued septic infection.

SYMPTOMS.—The incubation period varies from a few hours to seven days. The onset is usually sudden, with fever, and marked constitutional disturbance.

ERYSIPELAS OF OLDER INFANTS AND CHILDREN.—Except in the earlier months of infancy, the clinical course of erysipelas is very similar to that of adults, but in general milder and more favorable. The initial chill is usually absent, and constitutional disturbance is less marked, although vomiting is usually present, and occasionally delirium. The temperature is high at the onset, is usually continuous or slightly remittent for from four to eight days, and then falls by crisis or rather rapid lysis.

CHART 18



Erysipelas of legs. Female, 6 months old

The skin shows a sharply bounded area of redness on the face, trunk, or extremities. This area is swollen, hot, often tender, and the surface is tense and often glazed. Vesicle formation is common. In facial erysipelas the features are characteristically altered by the swelling. The spread of the disease is rapid, and the boundaries continue to be sharply defined. The swelling and redness usually disappear, and desquamation begins, in the area first affected, while the disease is still spreading at the margin. The adjacent lymph nodes are usually swollen and tender.

The spread of the disease may cease abruptly at any time, with a fall of temperature. Occasionally the process may progress further,

and advance over a large part of the body, but this type (*erysipelas migrans*) is more often seen in early infancy.

ERYSIPELAS OF EARLY INFANCY.—When the disease occurs in the early months of life, its beginning is usually accompanied by cold extremities and collapse. The temperature is raised, and the higher its degree the graver the prognosis. The temperature curve, as a rule, is intermittent, with considerable morning and evening variations, except in the more severe forms, in which there is continued high fever; in the latter cases icterus is apt to develop.

The efflorescence, although at times similar to that which is seen in the adult, usually differs somewhat on account of the more delicate structure of the infant's skin. It begins as a *faint erythema*, which spreads rapidly and as quickly disappears, sometimes within twenty-four hours, and twenty-four hours later desquamation may occur. In the meantime spreading continues at the margin, the area of redness and swelling being a very narrow one, and swelling being often imperceptible. These same appearances are seen at times in older infants and children who are very anemic or poorly nourished.

In some cases in young and poorly nourished infants, fever may be slight or entirely lacking. In these cases the small rapid pulse and marked prostration show that the disease is not less severe.

It is in early infancy that the prolonged cases of *erysipelas migrans*, in which the process wanders over a great part of the body, are most often seen.

ERYSIPELAS OF THE NEWBORN.—Erysipelas is a less common manifestation of infection of the newborn than is general sepsis. Infection usually occurs through the umbilicus, but may occur through any other point of abrasion. It does not usually occur at birth, but in the week following birth.

Although the temperature in the early hours or even days of the disease may not be raised, yet, as a rule, fever soon appears, the temperature varying from 102° to 105° F. Reddening and swelling, not of a high grade at first, appear on the part affected. The infants show symptoms of a general sepsis. Vomiting frequently occurs, followed by collapse and, almost without exception, by death.

COMPLICATIONS.—In young, poorly nourished, or rachitic infants, the most common serious complication is bronchopneumonia. General sepsis is rare as a complication of erysipelas. Subcutaneous abscesses are sometimes seen. A peculiar widespread edema has been observed to follow the healing of some cases of erysipelas.

DIAGNOSIS.—The diagnosis is usually easy, depending mainly on the rapid extension and sharp boundaries of the cutaneous inflammation, with the associated febrile disturbance. Acute facial eczema, and acute cellulitis (subcutaneous lymphangitis) present the most

difficulty in differential diagnosis. Neither condition shows the sharp raised boundaries characteristic of erysipelas. There are, however, intermediate types between erysipelas and lymphangitis, especially on the scalp.

PROGNOSIS.—The prognosis depends upon the age and general condition of the patient. In strong, well nourished infants, and in older children, the prognosis is good, in general better than in adults. Severe cases with high fever, intense inflammation of the skin, great restlessness, delirium, and somnolence, leading to death, are rare.

In the newborn, in very young infants, and in weak, poorly nourished infants, the prognosis is very grave. In the newborn the disease is almost invariably fatal.

PROPHYLAXIS.—Cleanliness, and the aseptic treatment of wounds and ulcers, are the chief measures of prevention against erysipelas. Such measures are particularly important in the care of the umbilicus in newborn infants. It is well not to allow children with open wounds or abrasions to come into contact with cases of erysipelas.

TREATMENT.—The treatment of erysipelas is in general that of any acute self-limited disease. Severe cases with circulatory depression require appropriate stimulation. None of the drugs formerly advocated for internal use has given evidence of any real value.

For local application, almost every remedy in the pharmacopeia has been advocated. The disease is so extremely erratic in its course, that no convincing evidence can be obtained as to the value of any particular remedy. The favorite preparation is *ichthyol ointment* in ten to twenty-five per cent strength. This is spread on muslin, and covered with gutta-percha tissue to prevent drying. A fresh application is made daily.

In severe cases, vaccine therapy may be tried. There is no positive evidence of its value, but it can do no harm. An autogenous vaccine, made from a culture taken from the lesions, should be used whenever there is anyone within reach who is master of the technique. Otherwise, a stock streptococcus vaccine must be used.

PROBLEMS AND RESEARCH.—The chief problem in erysipelas has to do with the possibility of a specific therapy. This must depend upon the continued study of the streptococcus group of micro-organisms. The difficulties attending this work have already been summarized under Rheumatic Fever.

The serum treatment of streptococcus infections has certainly not proved successful. The weight of evidence is against its value. This is probably due to the multiplicity of strains which compose the streptococcus group, and to the probability that a serum is only effective against its own particular strain.

The same difficulty militates against the success of stock vaccines. Whether or not autogenous vaccines have any effect upon the course of the disease is an unsettled question. The most extensive report on vaccine therapy in erysipelas is that of Erdman, based on 800 cases. The evidence in this report is wholly against the value of vaccine therapy.

VI. CHRONIC INFECTIOUS DISEASES

TUBERCULOSIS

Tuberculosis is an infectious disease, caused by the *bacillus tuberculosis* of Koch.

Tuberculous infection may occur at any age. Owing to the fact that the pathology and clinical manifestations in early life are widely different from those of adult life, tuberculosis was formerly believed to be rare in infancy. This has been shown to be untrue, and it has come to be recognized that tuberculosis is the most important chronic disease of infancy and childhood.

Numerous statistics have been collected in recent years tending to show the frequency of tuberculosis in the various years of infancy and childhood. These tabulations show a wide variation according to the locality in which they were collected, the European figures being notably higher than those from this country. Moreover, such statistics give no really exact information as to the frequency of tuberculosis in infancy and childhood. Some tabulations are based on the number of deaths from tuberculosis per 10,000 of the living. These statistics are not, however, an accurate measure of the frequency of tuberculosis in early life, but are rather a measure of its tendency toward a fatal ending at the different ages. It is well known that infants are especially liable to severe acute forms of tuberculosis, while in middle childhood various subacute and chronic secondary forms which do not tend to end fatally are particularly common. The number of deaths from tuberculosis per 10,000 of the living is highest in the first year of life, and remains high during the second year. After the second year it falls rapidly, reaching a minimum in the period between five and ten years of age. After this age it again rises, reaching in the period of twenty to twenty-five years approximately the same figures as those seen in the first year. It continues to rise until a maximum is reached at sixty years.

Other tabulations are based on the percentage of autopsies at which tuberculosis has been found on careful examination. Here again the statistics are no accurate measure of the general frequency of tuberculosis among children, because the tuberculosis may be the direct or contributory cause of death, or it may be an accidental finding having no bearing on the cause of death. The figures in general show a very low percentage of tuberculosis at autopsy in the

first three months of life, which rises rapidly in the second three months, and continues to rise throughout childhood. Hamburger's figures are as follows:

TABLE 59
Percentage of Tuberculosis at Autopsy

AGE	PER CENT
Under 3 months.....	4
3- 6 months.....	18
6-12 months.....	23
1- 2 years.....	40
2- 4 years.....	60
4- 6 years.....	56
6-10 years.....	63
10-14 years.....	70

The figures in this country are notably lower than those in Europe.

There is no satisfactory way of determining the frequency of tuberculosis among children in general. The clinical manifestations are entirely too doubtful to form a basis for any estimate. As to the cutaneous tuberculin reaction, von Pirquet and other observers believe that in childhood an accurate estimate of the frequency of tuberculosis in apparently healthy children can be made by this means. The reports have been so widely divergent, however, that we must consider the diagnostic value of the various tuberculin reactions as still unsettled.

ETIOLOGY

TYPES OF BACILLI.—The tubercle bacillus, like many other pathogenic microorganisms, has a number of distinct types or strains. Most important among these are the so-called human and bovine types, which are distinguishable one from another by animal inoculation experiment. The bovine type is that commonly associated with tuberculous disease in cattle. As milk forms so large a part of the food of young infants, some observers have maintained that the frequency of tuberculous disease in infants is due to their liability to infection with bovine bacilli from contaminated milk. Other authorities have denied that bovine bacilli can infect human beings. This question has formed an important subject of research and discussion. In reviewing all the literature, the following conclusions can be drawn: 1. Both the human and the bovine types of tubercle bacilli can infect infants and children. 2. The relative frequency of human and bovine infection is widely variable in different localities, the variability probably depending on the frequency of tuberculous disease in cattle, on the efficiency of cattle inspection, and on the use of raw or pasteurized milk. 3. In most localities, infection with the human type of bacillus is by far the commoner.

PREDISPOSING CAUSES. AGE.—Age is generally considered the most important of all the factors predisposing toward tuberculous infection. This opinion is based on the frequency of tuber-

culosis in early life, on the fact that in the great majority of cases in which tuberculosis appears in adult life, the original infection was contracted in childhood, and on the fact that the normal adult appears to be comparatively immune. This explanation does not seem entirely conclusive. Postmortem statistics show that infection with tuberculosis is rare in the first three months of life, but shows a great increase in frequency as the infant begins to come more in contact with its surroundings, and from this time on, the frequency of tuberculous findings at autopsy increases steadily. It seems most probable that the human being in general is predisposed toward the tuberculous infection, in the sense that when exposed to virulent bacilli, he will contract the disease. Exposure becomes frequent as soon as the infant comes in contact with his surroundings, and continues to be frequent throughout childhood. Consequently, tuberculosis is usually acquired in childhood, not because children are more susceptible, but because exposure to infection usually occurs before adult life is reached. The apparent immunity of adults to fresh infection may be explained on the hypothesis that these adults may have become infected in childhood, and having successfully resisted the disease, have acquired an immunity. The variations in the fatality are best explained by the hypothesis that resistance, not against infection, but against the spread of the disease in the body, is developed in middle childhood. For a proper understanding of the phenomena of tuberculosis in early life, it is essential to distinguish sharply between resistance against the occurrence of infection, and the resistance which all human beings develop after the occurrence of infection, through the defensive mechanism possessed by their bodies. The former resistance, in my opinion, does not exist, or at most, is an unimportant factor. The latter resistance is all-important.

HEREDITY.—It has been believed from early times that an inherited predisposition toward tuberculosis is a most important factor. This belief is based on the frequency of tuberculous infection in the children of tuberculous parents. The most modern views on tuberculosis deny that any specific susceptibility toward tuberculous infection can be transmitted by inheritance. The frequency of tuberculosis in the children of tuberculous parents can be explained far more satisfactorily on the basis of *exposure to contagion*. There is no evidence that the puny offspring of parents who have suffered from tuberculosis, or other chronic or constitutional diseases, are more susceptible to the original tuberculous infection. It is however probable that in such children the capacity of developing resistance through their defensive mechanism is impaired.

POVERTY AND CROWDING.—This is an important predisposing cause in the tuberculosis of early life. Wherever human beings live

in close contact, the opportunities for the transmission of any disease by contagion are greatly increased. Unsanitary surroundings increase the chance of infection by contagion, and decrease the chance of successful resistance when infection has once occurred. Tuberculosis in the bread-winner of the family increases the poverty and crowding, and every opportunity is afforded for the rapid dissemination of tuberculosis among the younger numbers of the family, in whom, the capacity for resistance being weakened by absence of sunlight and fresh air, the disease tends to run a severe course.

ACUTE INFECTIOUS DISEASES.—The occurrence of certain acute infections, particularly measles, whooping-cough, and influenza, are so often rapidly followed by the appearance of clinical manifestations of tuberculosis, that an etiologic connection cannot be doubted. The nature of the connection has been variously explained, as follows: 1. That the acute infection increases the constitutional susceptibility of the child toward tuberculous infection. 2. That these acute infections produce pathological conditions in the mucous membranes and lymphnodes, thus preparing a favorable soil for tuberculous infection. 3. That they diminish the resistance against the spread of an already existing infection. There is no definite evidence in favor of the first two explanations, and in my opinion the liability of any child to tuberculous infection does not depend on variations in constitutional susceptibility, nor upon variations in the condition of mucous membranes and lymphnodes, but entirely upon whether or not the child is sufficiently *exposed to infection with virulent bacilli*. On the other hand, I believe the third to be the true explanation of the frequent appearance of clinical tuberculosis after acute infections. There is evidence also in support of such an explanation. It has been shown that in certain acute infections there is a period, called by German writers “die anergische Periode,” in which there is a lowered capacity of resistance. This has been notably demonstrated in measles, in which, for about a week, the tuberculin reaction is greatly diminished in intensity or disappears, and it is at this time that widespread clinical symptoms of tuberculosis are apt to appear. It seems quite probable that a similar phenomenon occurs in other acute infections, and that it explains the frequent appearance of severe tuberculous manifestations following such infections.

MODES OF TRANSMISSION OF THE INFECTION. INTRA-UTERINE INFECTION.—Congenital tuberculosis, though rare, can occur, as has been shown by a number of well-authenticated reports. In most cases the mother was suffering from advanced tuberculosis, and the mechanism of transmission was through tuberculous disease of the placenta. Children infected thus during fetal life are usually

either still-born, or die in the early months of infancy. Such infection has little bearing on the clinical tuberculosis of infancy and childhood.

DIRECT INOCULATION.—Tuberculosis can be transmitted by direct inoculation, as is shown by numerous instances. The disease has been communicated by the bite of a tuberculous patient during the rite of circumcision, and by the hands of the physician or midwife during obstetrical practice. In comparison with other modes of transmission, infection by direct inoculation is rare.

CONTAMINATED FOOD.—The milk of tuberculous cattle can transmit tuberculosis to the young child. The frequency of bovine infection from contaminated milk is, as already stated, widely variable. In my own experience, milk infection is rare, but well-authenticated reports from some localities suggest that it may be quite common. The unpasteurized milk of tuberculous cattle will certainly not transmit tuberculosis to every child fed with that milk, and probably not even to the majority. On the other hand, it should be remembered that there is always danger of such transmission, and care should always be taken to avoid this possibility, either by pasteurization of milk supply, or by using milk of properly inspected cattle.

CONTAGION—Contagion is by far the most important factor in the transmission of tuberculosis. Tubercle bacilli are discharged in the greatest numbers in the sputum of adults suffering from pulmonary tuberculosis. They are discharged in smaller numbers and in much greater dilution, in the urine, feces, and milk, and in the discharge of tuberculous abscesses. The sputum is the chief source of danger. Owing to the peculiar pathology of tuberculosis in early life, the tuberculous child is relatively of very slight importance as a source from which the infection is conveyed to other children. Sputum is not expelled in early childhood, and few if any bacilli are expelled in coughing. Indeed, the lesions of tuberculosis in early life are of such a character, that the tubercle bacilli are usually kept imprisoned, and cannot be conveyed to other children. Only such children as have some discharging tuberculous lesion are really dangerous as sources of infection, and even in them the danger is less than from the adult consumptive.

It has been shown that tubercle bacilli may be conveyed directly from one individual to another, through the medium of the moist drops expelled in coughing, or by kissing. Such drops may be expelled in a fine spray to a distance of eight or ten feet. From this spray, and from carelessness in disposing of the expectoration, clothing, bed-clothes, carpets, hangings, handkerchiefs, and similar articles in the child's surroundings may be contaminated by virulent bacilli in a moist state. Sputum may become dried without the bacilli

losing their virulence, and the bacilli may thus become part of the dust of the room. They may be introduced into the mouths of children by various objects contaminated with tuberculous sputum. The habit of infants of putting everything into their mouths increases the danger. The fact that the bacilli in dried sputum may be disseminated in dust, led to the theory, very prevalent at one time, that tubercle bacilli are so widely disseminated in nature, that everybody is exposed, and that the occurrence of infection is due to individual susceptibility, or to lowered resistance. Such a theory must presuppose that the bacilli retain their full virulence indefinitely. This is not true. Tubercle bacilli may retain their virulence for a considerable time in dust, but not indefinitely. They retain their virulence better when in houses, away from sunlight and fresh air. The evidence is pointing more toward a *comparatively close contact with the consumptive as the important factor in acquiring the disease*. The closer and longer the contact, the greater the danger. Next in importance to actual contact, is living in rooms or houses formerly occupied by a consumptive. There is comparatively little danger of acquiring the disease in hotel bedrooms and sleeping cars, or from the dust of the streets. In the majority of cases the source of the infection is some member of the household or some frequent visitor.

PORTALS OF ENTRY.—The tubercle bacilli can enter the body through any part of the skin or mucous membrane. The relative frequency of the various portals of entry is estimated from the lesions which at autopsy show evidences of being primary.

The lung is by far the most frequent portal of entry in infancy and childhood, the bacilli being inhaled. They may first be introduced into the mouth, and later inhaled from the throat. Probably in infants more bacilli are swallowed than are inhaled, but in the former case they must run the gauntlet of the gastric juice, and are usually destroyed in the stomach.

While statistical reports differ somewhat, the portal of entry standing next in frequency to the lung, is the mucous membrane of the intestinal canal. This is the usual portal of entry for bacilli of bovine origin, conveyed in contaminated food; also, bacilli of human origin can enter in this way in rare instances. Infection through the intestine is much less common than through the lung. Albrecht found it in only seven instances in 1,060 autopsies, and Gohn only three times in 189. It is more common in those localities in which infection of bovine origin is more common. Some authorities, believing in the greater significance of bovine than of human infection, have maintained that the intestine is the usual portal of entry in infancy. They are at once met with the objection that the bronchial lymphnodes are much more often found tuberculous at

autopsy than are the mesenteric, and show more frequent evidences of primary involvement when both sets are tuberculous. This objection has been answered on the theory that the tubercle bacilli entering through the intestine, pass through the mesenteric lymphnodes, and become localized in the bronchial lymphnodes as a point of least resistance. This explanation is highly improbable, and is not supported by any adequate evidence. All the evidence points toward the greater frequency of infection with bacilli of human origin, taken in by inhalation.

The tonsil stands third in frequency as a portal of entry, and may possibly be more frequent than the intestine, especially in later childhood. Reports show wide differences. Neither Albrecht nor Gohn found a single instance of primary tonsillar infection in his large series of autopsies. Other observers have reported the frequent finding of a primary lesion in the tonsil. Whether the existence of tuberculous cervical adenitis always means infection through the tonsil, or whether the infection is conveyed to the cervical lymphnodes from a primary infection in the lung, is still an open question. It is probable that infection through the tonsil is commoner in childhood than in infancy, and that this explains its rarity at autopsy, and the frequency with which the tonsils removed by operation are found tuberculous.

Infection through the skin, through the mucous membrane of the mouth or nose, and through that of the genito-urinary tract, has been observed, but instances are rare.

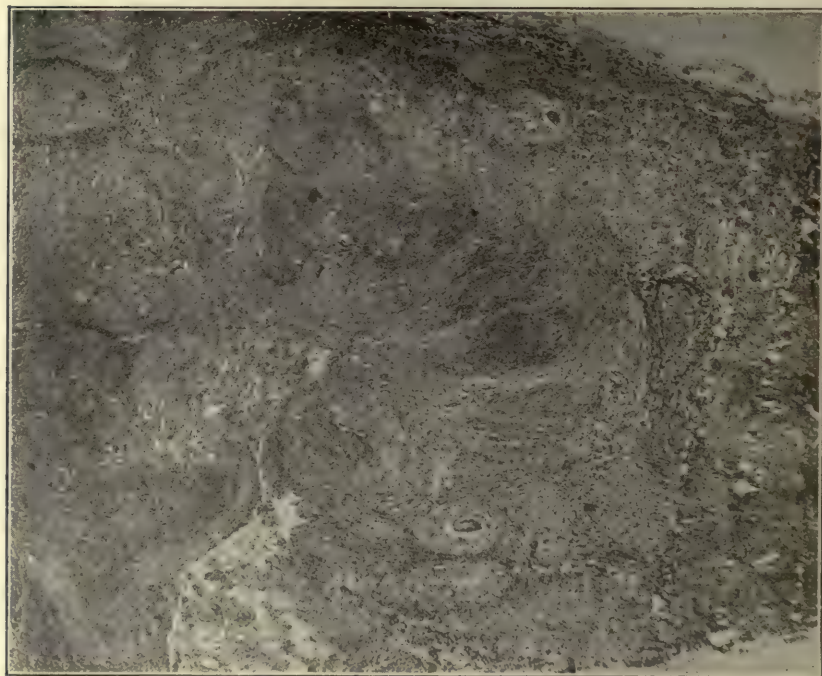
PATHOLOGY

THE PRIMARY LESION.—One of the most prolific subjects of discussion in the tuberculosis of early life is whether the tubercle bacillus causes a lesion at the portal of entry, or whether it passes through the mucous membrane without the formation of a local lesion, but causing a primary lesion in the lymphnodes. The chronic tuberculosis of early life is essentially a lymphnode process, and the characteristic pulmonary tuberculosis of adults is rare in childhood. From this fact has come the widely accepted teaching that the primary lesion is in the lymphnodes. Von Pirquet, basing his opinion on the researches of Albrecht and Gohn, states definitely that there is always a primary lesion at the portal of entry, and that when it is not found, a primary lesion in the lung has been overlooked. While this question is perhaps not definitely settled, I have become convinced that von Pirquet's statement is very close to the truth. In my experience, if careful search be made, a primary lesion may usually be found at the portal of entry. It is often so inconspicuous as to suggest that it might easily have been overlooked, and I believe that

in the few cases in which it is not found at the portal of entry, it is because it is overlooked.

The most common seat of the primary lesion is the lung. The lesion is easily distinguishable from the secondary pulmonary lesions, tuberculous bronchopneumonia and miliary tuberculosis, which are so common and conspicuous in infancy and early childhood. It is an area usually of a size varying from that of a small pea to that of a hazelnut. It is usually caseous, and the center may show either softening, or a small cavity. It is usually greyer than the yellowish-white caseation of the secondary lesions. Old primary lesions may

FIG. 155



Section through the primary lesion of tuberculosis in the lungs
It is to be noted that the alveolar outlines are completely obliterated

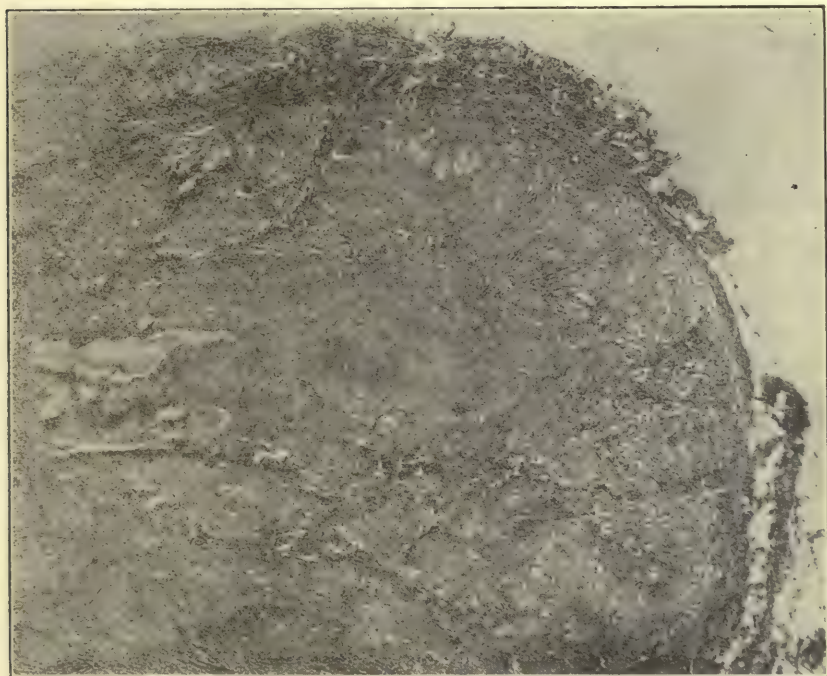
be surrounded by a fibrous capsule, and still older ones may be represented by a small fibrous area containing a little calcareous material. These latter are often very difficult to find. Around the periphery there is often a collection of yellowish-white miliary tubercles, suggesting direct extension of the process. Microscopically the primary lesion is distinguished from the secondary lesions with caseation, in that in the primary lesion no trace of lung structure is retained.

In the intestine, the primary lesion is an oval tuberculous ulceration of the mucous membrane. It is in no way distinguishable from

the secondary ulcerations of the intestinal mucosa which are caused by the swallowing of tuberculous sputum, and is recognized as being primary because either the mesenteric lymphnodes only are tuberculous, or they show a more advanced process than the lymphnodes of the chest. Also, in cases with primary tuberculosis of the intestine, no characteristic primary lesion is found in the lung.

In the tonsil, the primary lesion consists in conglomerate tubercle formation, and is usually not recognizable macroscopically.

FIG. 156



Section through the primary lesion of tuberculosis in the lungs
It is to be noted that the alveolar outlines are completely obliterated

THE ROUTES OF INVASION.—The tubercle bacilli tend to extend from the primary lesion, and to invade the body of the host. There are various routes by which this invasion takes place. The following are the commonest: 1. By the lymph channels; 2. By direct extension; 3. By the air passages; 4. By the digestive canal; 5. By the blood.

The first extension of the tuberculous infection is probably one which almost invariably occurs in infants and children, namely, to the lymphnodes by way of the lymph channels. While there has been some evidence afforded by animal experiments that the bacilli may pass through one set of lymphnodes to locate in another, this

probably does not occur in man. *The lymphnodes first affected are those nearest to the portal of entry*, which receive the lymphatics draining the region of the primary lesion. Consequently, in infection through the lung, the principal tuberculous lesions are found in the lymphnodes situated about the bronchi and the bifurcation of the trachea, while in infection through the intestine, the principal tuberculous lesions are found in the mesenteric lymphnodes. In tonsillar infection, it is the cervical lymphnodes which are involved.

The chronic tuberculosis of infancy and childhood is essentially a lymphnode process, and it is in the lymphnodes that the battle between the attacking parasite and the defending host is mainly waged. In many cases, the issue is settled in the lymphnodes, and tuberculous invasion goes no farther. Even when the defensive mechanism of the host is of a high efficiency, the bacilli are usually not all completely killed, but some remain alive in the center of the lesion, harmless, as long as they do not escape the boundaries set for them by the local reaction of resistance.

At times bacilli escape from their boundaries, and extending by various routes from the primary lesion or from the adjoining lymphnodes, reach other parts of the body and cause secondary tuberculous lesions. Children are particularly liable to such extension, and the younger the child, the greater is this tendency. Consequently it is in childhood that we see widespread secondary lesions of tuberculosis, which in infants are often of the most acute and fatal character. Age is the most important factor in determining the frequency of extension of tuberculous infection. As children grow older, more resistance is developed, and the secondary lesions first change in character, and then diminish in frequency. Other conditions, occurring in childhood, may cause a sudden lowering of the resistance against the extension of tuberculosis. Such a condition is seen in the occurrence of an acute infection with some other parasite. The resistance may be gradually lowered by various chronic diseases.

The bacilli may spread by direct extension from the primary lesion. The lesion grows larger by the formation of miliary tubercles about its periphery, and finally reaches the pleura, causing a *tuberculous pleurisy*, with serous or sero-fibrinous exudate.

The bacilli may enter the air passages, either from the tuberculous material of the primary lesion entering a bronchiole, or from the softening of a lymphnode breaking through into a large bronchus. Extension through the air passages causes *tuberculous bronchopneumonia*, which is a very common lesion in infancy, but which grows less common with advancing childhood.

The bacilli from the primary lesion may enter the digestive canal. This occurs particularly when there is an area of softening in the primary lesion, from which tuberculous sputum is coughed up. In-

infants and young children do not expectorate, but swallow this sputum. It is probable that in some cases tubercle bacilli from this source enter the tonsils or other lymphoid tissue of the pharynx, and are conveyed by the lymphatics to the *cervical lymphnodes*, where they set up a process similar to that seen in the bronchial lymphnodes. It is not known in what proportion of cases tuberculous cervical adenitis represents a secondary, and in what proportion a primary infection through the tonsil. The bacilli in the swallowed sputum are carried to the intestinal canal, where they may cause tuberculous ulceration of the mucous membrane. These secondary ulcers are usually multiple, and in appearance are indistinguishable from the primary intestinal lesion. From this *tuberculous iliocolitis*, whether secondary, or primary (bovine), the bacilli again following the lymph-channels, are carried to the mesenteric lymphnodes where they cause the usual chronic lesions. Further spreading may occur by direct extension to the peritoneum, in which case *tuberculous peritonitis* is seen.

Finally, the bacilli may enter the blood stream in large numbers. This is particularly liable to occur in infancy, and occurs less and less often as children grow older. When it occurs, the bacilli are widely disseminated throughout the body, and give rise to a more or less general *acute miliary tuberculosis*, which is a severe and fatal form particularly associated with early life. The miliary tubercles may be found in the lungs, spleen, and liver, and at times in various other organs. The tubercles are often carried to the brain, causing a *tuberculous meningitis*, or *acute miliary tuberculosis of the meninges*, which is very apt to determine the character of the clinical manifestations.

As children grow older, there is less tendency toward escape into the blood stream of a large number of tubercle bacilli, but occasionally bacilli may escape in small numbers, or possibly singly. Probably many bacilli thus escaping do not find an environment favorable toward their development, and are destroyed. At times, however, they lodge in some remote part of the body, where they can develop, and where the reaction of the tissue again gives rise to chronic tuberculous lesions. Examples of such extension are the tuberculosis of the bones and joints, the solitary tubercles sometimes seen in the liver or brain, and chronic tuberculosis of the genito-urinary organs.

The diagrams show the routes of invasion of the tubercle bacillus in childhood.

To understand the phenomena of tuberculosis in childhood, it is useful to look at the condition from the point of view of the parasite as well as from that of the host. It is the law of life for the parasite that it must enter the body of the host, and must also escape from the body in order to infect another individual. The tubercle bacillus in the child encounters comparatively little resistance at the portal

DIAGRAM SHOWING THE ROUTES OF INVASION OF TUBERCULOSIS
OF HUMAN ORIGIN

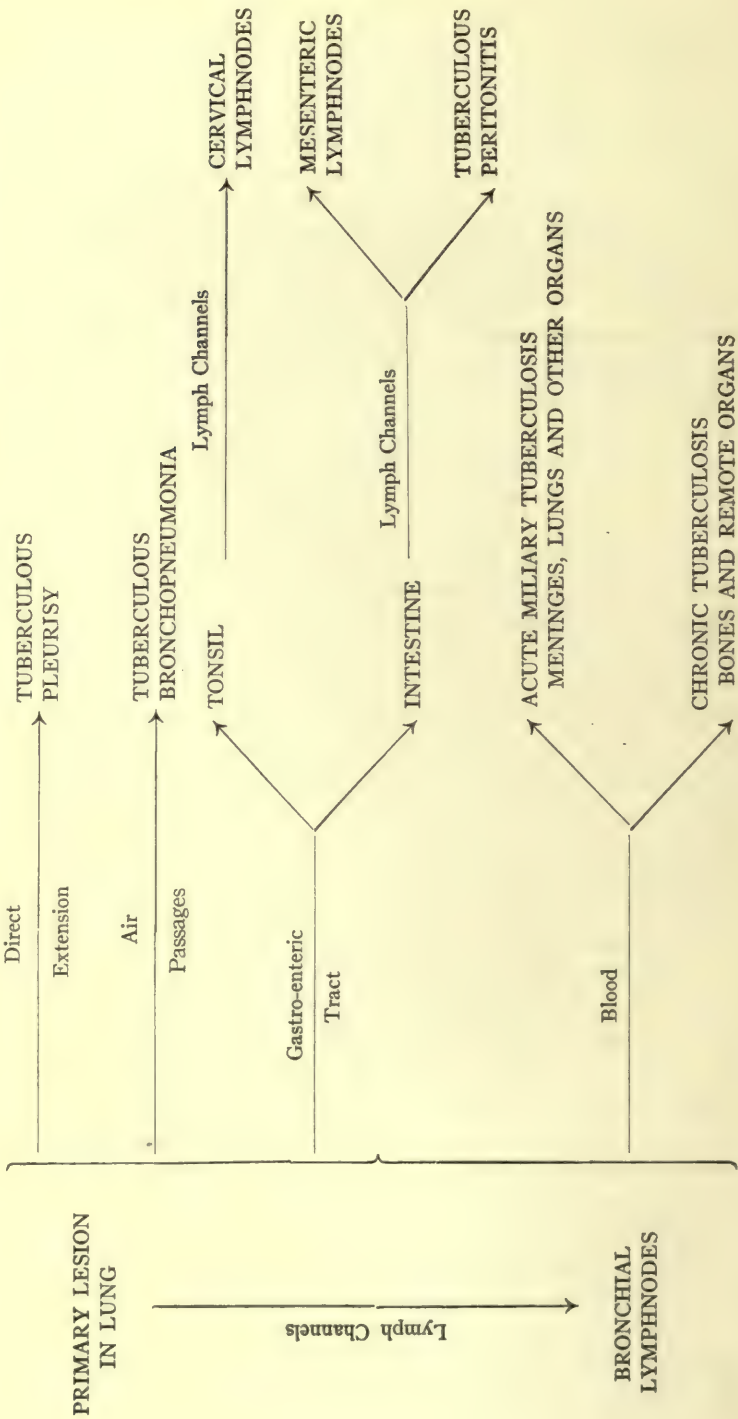
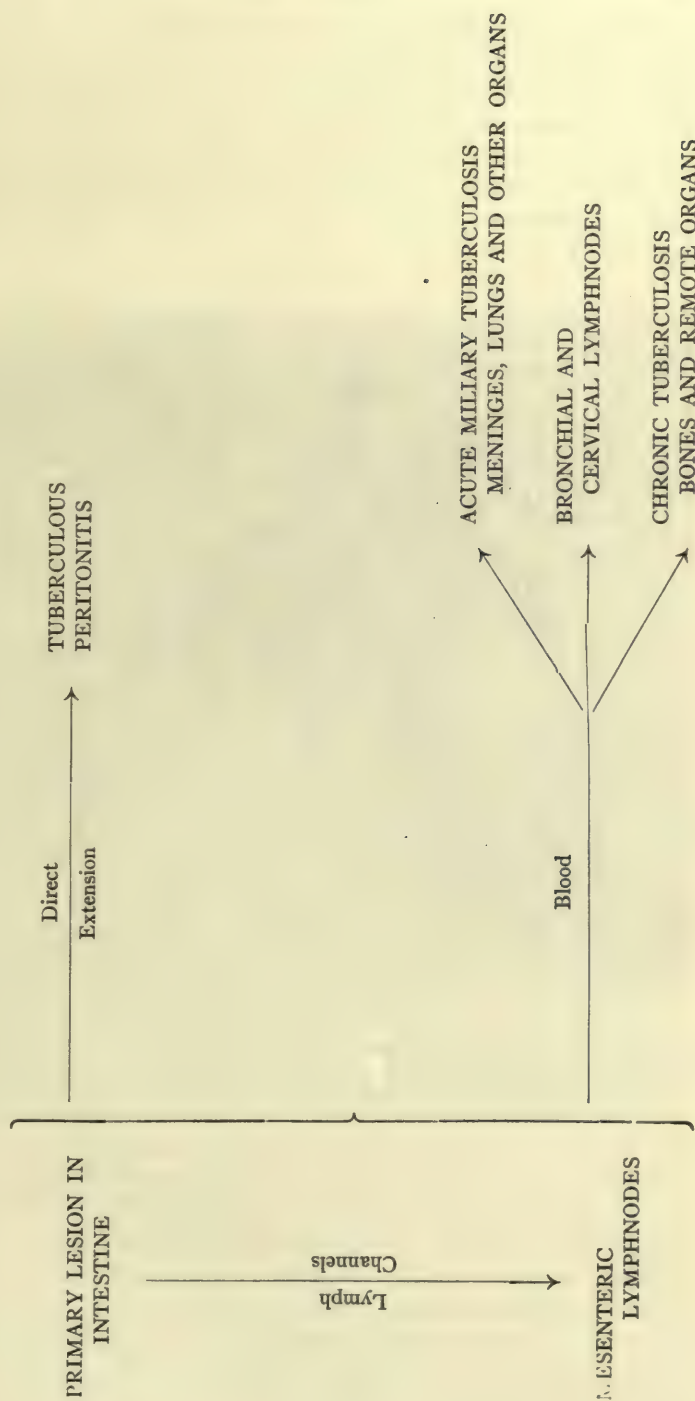
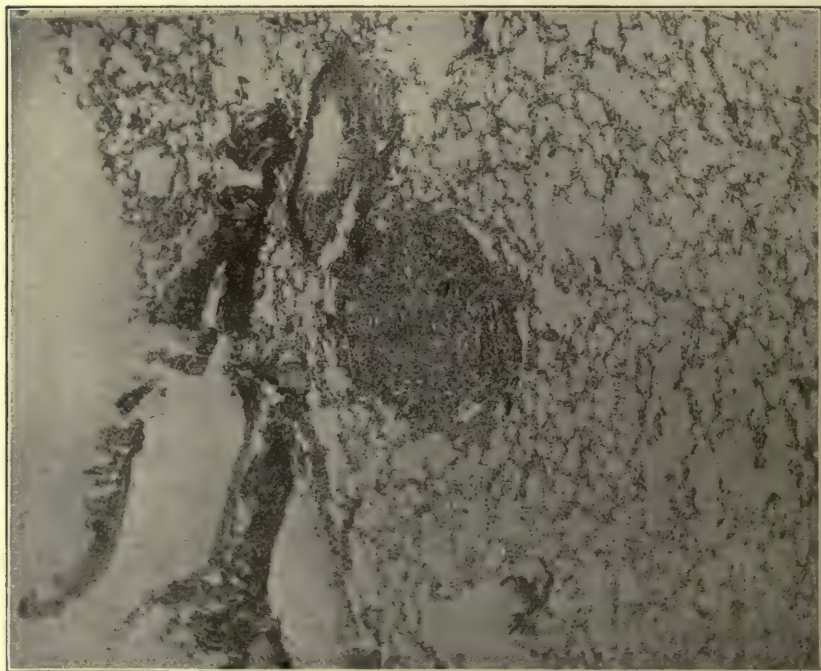


DIAGRAM SHOWING THE ROUTES OF INVASION OF TUBERCULOSIS OF BOVINE ORIGIN



of entry, and has great invasive power, penetrating deeply into the tissues of the host. As resistance develops, the conditions in these deeper lesions are unfavorable for the eventual escape of the parasite. As adult life is approached or reached, invasion is less easy, but the parasite must escape, and renews its activity in the lung at the portal of entry. The greater local tissue resistance at this point, while preventing invasion, is more favorable to the escape of the parasite in the sputum.

FIG. 157



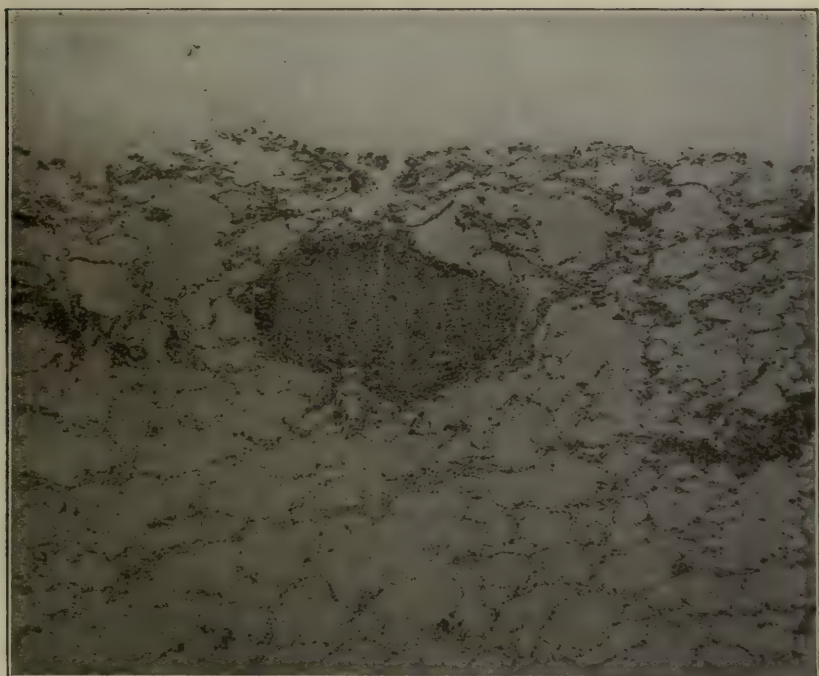
Miliary tuberculosis of the lung

Secondary lesion representing extension of the infection through the blood. It is to be noted that the alveoli surrounding the tubercle are free from exudate.

It is fairly definitely established by the experiments of Hamburger and others, that these chronic destructive lesions are only seen in individuals already infected with tuberculosis, and that the existence of such a preceding infection is the determining factor for the particular tissue reaction seen in chronic pulmonary tuberculosis. The only question is how the bacilli are conveyed to the lung. The theories are the following: 1. That chronic pulmonary tuberculosis represents a fresh aerogenous infection. 2. That it represents the tertiary reaction toward bacilli brought to the lung by the blood stream (Hamburger). 3. That it represents renewed activity in the original primary lesion.

The question as to whether the chronic pulmonary tuberculosis of adults represents a fresh aerogenous infection, or a lighting up of an old infection acquired in childhood, is still a subject of discussion. The majority of European observers (Behring, Hamburger, Römer, von Pirquet), and many in this country believe the latter theory to be the true one. Hamburger divides tuberculosis into three stages, the first represented by the primary lesion and the associated process in the lymphnodes, the second represented by all the secondary lesions produced by invasion, and the third represented by the chronic destructive lesions, such as the pulmonary tuberculosis of adult life, and the chronic tuberculosis of the bones and joints.

FIG. 158



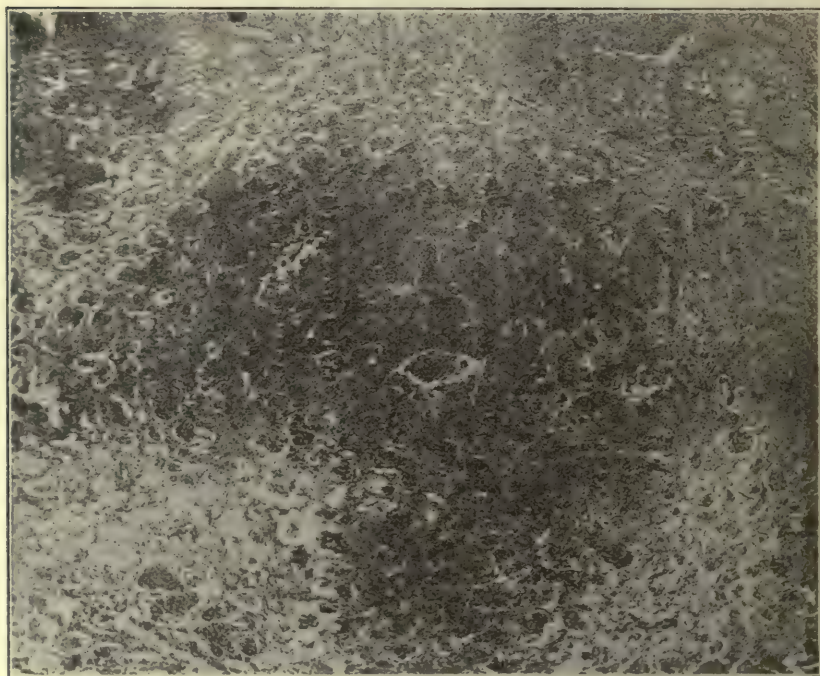
Miliary tuberculosis of the lung

Secondary lesion representing extension of the infection through the blood. It is to be noted that the alveoli surrounding the tubercle are free from exudate.

ANATOMY OF THE LESIONS. THE LYMPHNODES.—The lymphnodes usually involved when tuberculous infection occurs through the lungs, are usually spoken of as bronchial, but include three distinct groups. The first surrounds the trachea, the second is situated at the bifurcation of the trachea and surrounds the primary bronchi, while the third follows the course of the bronchi into the lung. These lymphnodes are enlarged to a varying degree. Sometimes all three

groups are involved, sometimes only the lymphnodes along the bronchi. One side is usually affected more than the other, the side most affected being that of the lung containing the primary lesion. Sometimes there are only two or three masses about the size of a hazelnut, while at other times there may be a mass two or three inches in diameter, surrounding the trachea and large bronchi, consisting of a large number of caseous glands fused together by inflammatory products. The mesenteric glands, when tuberculous, often form a still larger mass.

FIG. 159



Tuberculous bronchopneumonia

Secondary pulmonary lesion from extension through the air passages. This section shows an early stage of the process before necrosis has occurred.

These lymphnodes undergo the usual tuberculous changes, congestion, swelling, cell proliferation, and caseation. All degrees of the process may be found in them. A certain number of glands are usually caseous, of yellow appearance. Softening is common in the cervical lymphnodes, but comparatively uncommon in the bronchial and mesenteric glands, except in young infants. Calcification is fairly common, especially in older children. Bacilli may remain encapsulated in the lymphnodes for many years.

The enlargement of the bronchial lymphnodes may cause a variety

of comparatively rare secondary lesions. The pneumogastric and recurrent laryngeal nerves may be involved in the inflammatory process. The trachea, bronchi, and esophagus may be compressed or opened by ulceration. There may be ulceration into the air passages, or a mediastinal or retropharyngeal abscess may be formed.

THE LUNG.—The lung is the organ most frequently involved in the tuberculosis of infancy and childhood. Four distinct lesions are found in the lungs, the first being the primary lesion already described. The three secondary lesions are,—1. Miliary tuberculosis. 2. Tuberculous bronchopneumonia, and 3. Phthisis.

FIG. 160



Tuberculous bronchopneumonia.

Secondary lesion from extension through the air passages beginning necrosis in the center. Surrounding alveoli filled with cellular exudate.

In miliary tuberculosis of the lung, the infection is carried to the lung tissue through the blood stream. The tubercles may be found only in some part of the lung, or may be of general distribution. They are seen both upon the pleural and upon the cut surfaces, and appear as small, circular areas, varying in size from that of a pin-point to that of a pin-head or larger, of yellowish, greyish, or "sago body" appearance. Microscopically these tubercles are clear cut, and there is no exudate into the surrounding alveoli, unless there is

present in addition a simple or tuberculous bronchopneumonia. Miliary tuberculosis of the lung usually is seen in cases having a general miliary tuberculosis, with tuberculous meningitis.

Tuberculous bronchopneumonia is the most frequent secondary pulmonary lesion found post-mortem in infants and young children. This condition is characterized by the formation of caseous nodules of various sizes, or of large caseous areas. Both lungs are involved,

FIG. 161



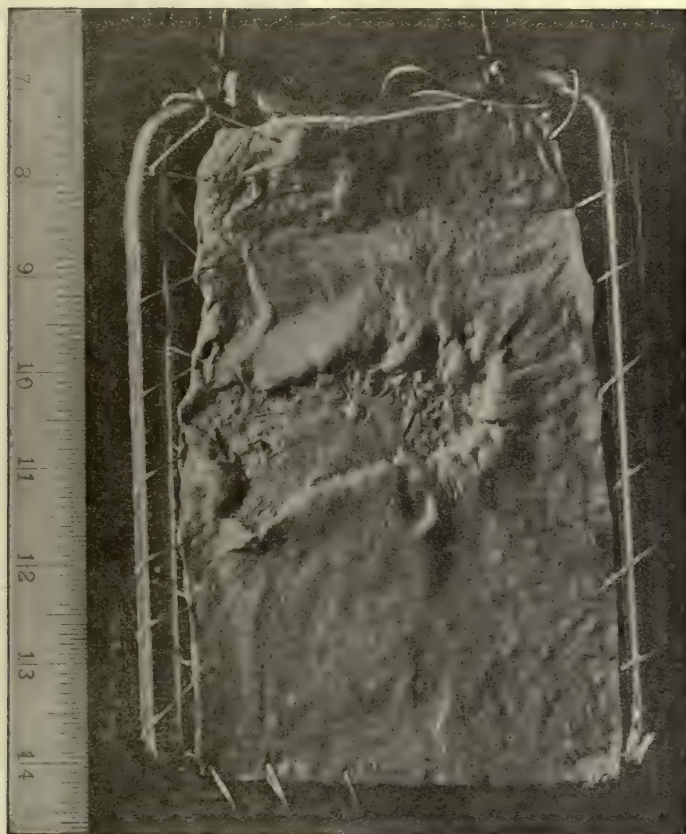
Tuberculous bronchopneumonia

This process represents the secondary pulmonary lesion in which extension of the infection has occurred through the air passages. It will be noted that the topography of the lung is not obliterated, and that the alveoli surrounding the caseous areas are filled with cellular exudate.

one usually more than the other. There is a cellular exudate in the bronchioles, and in the alveoli surrounding the areas of caseation. Large areas of caseous consolidation may be found, which sometimes include an entire lobe, or there may be several large areas in various parts of the lungs. There may be more or less extensive areas of softening in the caseous portions. The pleura is usually involved, the commonest lesion being dense fibrous adhesions binding the lung to the chest wall, or marked thickening of the pleura, with some caseation.

Microscopic examination shows that these cheesy nodules usually begin as tubercles in the walls of the small bronchi. The alveoli surrounding the focus become filled with inflammatory exudate, to which the tuberculous caseation extends, thus forming the larger nodules. Still larger areas are formed by the conglomeration of several discrete areas.

FIG. 162



Large tuberculous ulcer of cecum

Chronic pulmonary tuberculosis, or phthisis, is a rare lesion in childhood. There is usually much old fibrous tissue formation about the lesion, which in the center shows areas of caseation, softening, or cavity formation.

THE PLEURA.—The commonest lesion seen is a deposit of miliary tubercles upon the visceral pleura. Second in frequency is the formation of dense fibrous adhesions between the lung and the chest wall. The pleura may be markedly thickened with some caseation. In some cases a fresh fibrinous exudate is seen at autopsy. Serous pleurisy is comparatively rare in infancy and early childhood. Empy-

FIG. 163



Tuberculous ulcers of colon
 Female, 8½ years old
 Museum of the College of Physicians
 and Surgeons, New York.



Tuberculous ulcers of small intestine
 Female, 2¾ years old
 Museum of the College of Physicians
 and Surgeons, New York.

ema, pneumothorax, and pyo-pneumothorax are all very rare lesions in the tuberculosis of early life.

THE INTESTINE.—The fully developed lesion in the intestine is a tuberculous ulceration. In their early stages, small yellowish tubercles appear upon the mucous membrane, usually in the region of the Peyer's patches. The ulcers are irregular in shape, the long axis being at right angles to that of the intestine. They have raised, undermined edges, with ragged, greyish bases covered with granula-

FIG. 164



Tuberculous ulceration of the intestine

This ulcer represented the primary lesion in this case, but is histologically indistinguishable from secondary intestinal ulcers originating from swallowed sputum.

tions. On the peritoneal surface, there is a congestion, and usually a collection of small yellowish nodules over the seat of the ulcer. The ulcers may involve only the mucosa, or may extend into the deeper layers. Perforation is comparatively rare, and when it does occur, is not into the general peritoneal cavity, as a localized inflammation forms adhesions. The ulcers may heal by fibrous cicatrization, causing puckering of the intestinal wall, and sometimes narrowing of the lumen.

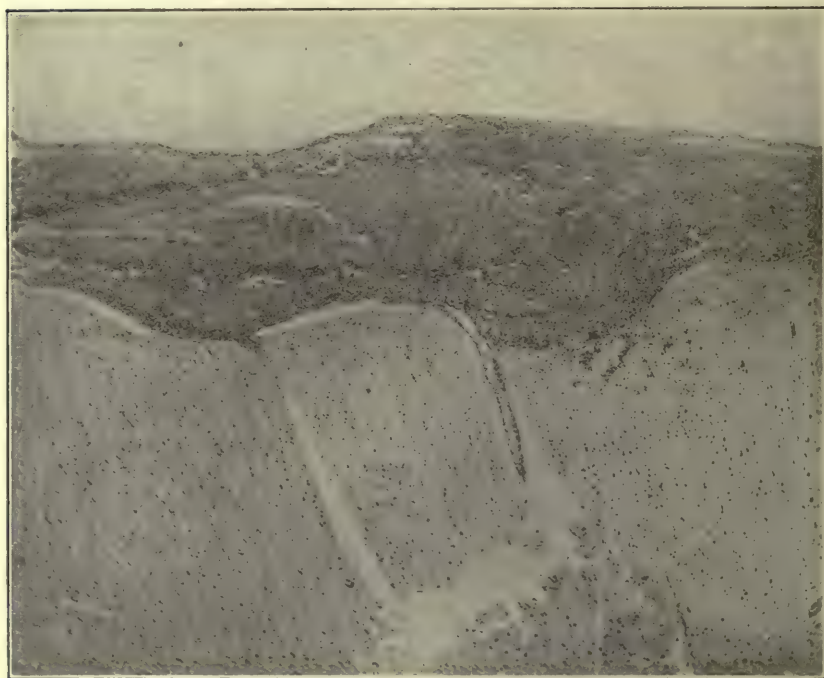
There is no anatomical distinction between tuberculous ulceration of the intestine representing the primary lesion, and that second-

ary to the swallowing of tuberculous sputum. In the latter case the ulcers are always multiple, and may vary in number from five or six, to fifty or sixty. In the former case the ulcers may be either single or multiple. The ulcers are seen most frequently in the small intestine, but sometimes the colon is involved.

Whenever intestinal lesions are present, there is always tuberculosis of the mesenteric lymphnodes.

THE PERITONEUM.—The peritoneum shows three varieties of tuberculous lesions. The first is a miliary tuberculosis without

FIG. 165



Tuberculous meningitis
Section shows a miliary tubercle of the pia mater

exudate, in which there is seen on the peritoneum, small greyish miliary tubercles. These tubercles are usually sparsely scattered, are not of general distribution, but are seen only in some localities, and there is little or no evidence of inflammation. This process represents only a part of a general miliary tuberculosis, in which the bacilli are conveyed to the peritoneum through the general circulation, and has no clinical significance.

The second form is a miliary tuberculosis with inflammation and exudation. The peritoneum of the omentum, mesentery, and viscera

is thickly strewn with discrete or conglomerate tubercles, and shows evidences of inflammation. There is congestion, some fibrin formation, and a profuse serous exudate, which usually gives rise to a marked ascites. This form is caused by extension of the infection from lesions of the intestine or of the mesenteric lymphnodes.

The commonest form is produced in the same way, by extension, but is much less acute than the ascitic form. There is tuberculous inflammation of the peritoneum, in the products of which efforts at repair take place, by the formation of fibrous tissue. The result is firm fibrous adhesions, which bind the intestinal coils one to another, and to the omentum, viscera, and abdominal walls. There may be serous, sero-purulent, or purulent exudate. There is usually marked fibrous thickening of the omentum. In the fibrous exudate between the intestines, and in the mesentery and omentum, there may be caseous nodules, or large caseous masses, some of which may show softening, and may even cause abscesses opening externally.

CHRONIC METASTATIC TUBERCULOSIS.—These lesions are caused by the transmission through the blood stream of tubercle bacilli, which cause chronic tuberculosis in various parts of the body. The commonest form of this variety of tuberculosis is the well-known tuberculous disease of the bones and joints. Other examples are the solitary tubercles sometimes seen in the brain and liver.

ACUTE MILIARY TUBERCULOSIS.—This is a common termination of tuberculous infection in infancy and early childhood. It is caused by a widespread general dissemination of the tubercle bacilli through the blood stream. Numerous small miliary tubercles are found in various organs. The organs most commonly involved are the lungs, brain, liver, and spleen. At times miliary tubercles are found in the kidneys, adrenals, heart, and other organs.

The lesions in the brain, which primarily involve the meninges, are interesting. In some cases, the surface of the brain is more or less thickly studded with miliary tubercles, without evidence of exudate between the tubercles. This is strictly a miliary tuberculosis of the meninges, rather than a tuberculous meningitis, although the two conditions have the same clinical manifestations. In other cases there is in addition to the miliary tubercles more or less extensive inflammatory exudate, showing itself either by cloudiness along the course of the vessels, or by the actual formation of fibrinous deposits. This is actually a tuberculous meningitis. In the former case, it is probable that each tubercle is formed by bacilli brought by the blood stream, while in the latter case, there is local extension of the infection from one area to another.

Both processes are apt to involve the base of the brain more than

the convexity. In both there is increased formation of cerebro-spinal fluid.

CLINICAL TYPES OF TUBERCULOSIS

The clinical manifestations of tuberculosis in early life, may for convenience of description, be divided into chronic, subacute, and acute. The following clinical classification may be made:

1. Chronic
 1. Common Primary Tuberculosis
 2. Cervical Adenitis
 3. Ileo-colitis and Tabes Mesenterica
 4. Bone-joint Tuberculosis
 5. Solitary Tubercle of the Brain
 6. Phthisis
2. Subacute
 1. Tuberculous Bronchopneumonia
 2. Tuberculous Pleurisy
 3. Tuberculous Peritonitis
3. Acute
 1. Tuberculous Meningitis
 2. General Miliary Tuberculosis

The majority of these clinical forms of tuberculosis show symptoms which depend upon the particular part of the body involved, rather than any symptoms distinctive of tuberculous infection as contrasted with other infectious processes of the same parts of the body. They are therefore more conveniently described under the diseases of the various organs affected, where the symptoms may be easily compared with those caused by other diseased processes. Only two clinical forms have no distinctive manifestations. These are the first, *chronic primary tuberculosis*, and the last, *general miliary tuberculosis*.

Common Primary Tuberculosis.—By common primary tuberculosis is meant the condition corresponding to the first stage of European writers, in which the process is confined to the primary lesion at the portal of entry and the adjacent lymphnodes. Invasion and wide-spread dissemination have not taken place to an extent sufficient to produce distinctive clinical manifestations. This form will be described in this division.

Cervical Lymphadenitis.—This form of chronic tuberculosis is clinically distinct, in that the involvement of the cervical lymphnodes is easily recognized by physical examination, and forms the most notable clinical feature. This will be described under diseases of the Lymphnodes.

Ileo-Colitis and Tabes Mesenterica.—These forms, whether representing primary or secondary infection, are distinctive in that the

most notable symptoms point toward the abdominal cavity. They will be described under the diseases of the organs involved.

Bone-joint Tuberculosis.—This form represents extension of the tuberculous process through the circulation. Bacilli lodging in bony tissue, set up a chronic tuberculous process, of which the clinical manifestations are distinctive. It will be described under diseases of the bones and joints.

Solitary Tubercle of the Brain.—By similar extension, chronic tuberculous processes may be set up in other parts of the body. In many cases these solitary tubercles have no distinctive clinical symptoms, and form only a part of the chronic tuberculosis of early life.

FIG. 166



Tuberculous dactylitis

Solitary tubercle of the brain, however, gives the clinical manifestations of brain tumor, and will be described under diseases of the brain.

Phthisis, or Chronic Pulmonary Tuberculosis, corresponds to the third stage of European writers, and is usually recognizable clinically. It will be described among the diseases of the lungs.

Tuberculous Bronchopneumonia, is the commonest secondary lesion of infancy and early childhood. It is usually clinically recognizable as a bronchopneumonia, and will be described under that heading.

Tuberculous Pleurisy, is similarly clinically evident as a pleurisy, and will be described under that heading.

Tuberculous Peritonitis, is another clinically distinct secondary manifestation of tuberculosis, and will be described under diseases of the peritoneum.

Tuberculous Meningitis, while usually only a part of a more or less generalized miliary tuberculosis, has a very distinctive clinical picture, which entitles it to separate consideration. It can be most conveniently described with the other forms of meningitis.

General Miliary Tuberculosis.—Under this heading will be included those cases which do not show the distinctive clinical manifestations of tuberculous meningitis. This form will be described in this division.

FIG. 167



Tuberculous dactylitis
Showing the involvement of the bone

THE CHRONIC TUBERCULOSIS OF EARLY LIFE

SYMPTOMS.—There are no diagnostic symptoms of chronic tuberculosis in infants and growing children. The disease may exist without any clinical manifestations whatever. Such cases are most commonly met with in infants. In older children, there is usually some secondary extension of the tuberculous infection, which gives more notable clinical manifestations. On account of this peculiarity of the chronic tuberculosis of early life, an early diagnosis is not often made. Most of the descriptions of tuberculosis in infancy and childhood enumerate symptoms caused by secondary extension of

the tuberculous infection. While such definite symptoms are of the greatest value in making a diagnosis of tuberculosis in a child, they do not aid in the recognition of the disease in its early stages.

GENERAL SYMPTOMS.—There are three general symptoms associated with chronic tuberculosis in infancy. These are *fever*, *emaciation*, and *anemia*. Fever is more commonly absent than present, unless extension of the infection has occurred. The temperature can show characteristic evening rises, but this is unusual, and fever, when present, is usually irregular, and often the temperature shows but little elevation above the normal.

The most common symptoms are those of failing nutrition. The infants may be pale and thin, and do not gain in weight. Changes in the composition of their food, made with the object of making them gain in weight, are unavailing. They are apt to show a particular difficulty in the digestion and absorption of fat. Finally, they begin to lose steadily, and become still more anemic. They are also often subject to bronchitis. It must always be remembered however, that chronic tuberculosis is quite compatible with a normal gain in weight. In my experience, emaciation and anemia are more often absent than present. In more than half the autopsies at the Infants' Hospital of infants dying from tuberculosis, the general nutrition was good.

The primary lesion does not often give rise to recognizable physical signs. The principal lesion in this chronic stage of the disease is tuberculosis of the lymphnodes. The following symptoms are associated with tuberculosis of the bronchial lymphnodes, but it must be remembered that any or all of them may be absent.

COUGH.—When present, the cough is loud, ringing, and metallic, and is sometimes paroxysmal. In some cases it may strongly suggest beginning whooping-cough. In whooping-cough, however, the cough changes its character, and becomes associated with characteristic paroxysms, with whoop, and with vomiting. The cough of bronchial gland tuberculosis does not change.

EXPIRATORY DYSPNEA.—This symptom, while much more often absent than present, is occasionally quite marked and characteristic. It is caused by pressure of the enlarged lymphnodes upon the bronchi and trachea, and is seen most frequently in young infants. The severity of this symptom is very variable. In marked cases the expiration seems prolonged and forcible, and is accompanied by a loud stridor, while inspiration is hardly perceptible. The rate of respiration is not increased to any extent, and the expiratory stridor may be scarcely perceptible when the child is quiet, but appears after crying or coughing.

INTERSCAPULAR DULNESS TO PERCUSSION.—The enlarged bron-

chial lymphnodes are often entirely unrecognizable on physical examination, giving no alterations to auscultation and percussion. In many cases, however, there is dulness in the interscapular region behind, and this, when distinct, is a very important sign. Much less frequent is dulness over the upper part of the sternum in front. Any dulness to the right or left of the sternum is usually due to an accompanying bronchopneumonia. Interscapular dulness should be carefully looked for in every suspected case. At times the dulness in this region caused by enlarged bronchial lymphnodes amounts to no more than an extension downward of the normal dulness of the cervical spine so as to involve the upper dorsal spine.

FIG. 168



Examination for D'Espine's sign

D'ESPINE'S SIGN.—D'Espine has described a sign of use in the recognition of enlargement of the bronchial lymphnodes which is of the highest importance in the diagnosis of the latent tuberculosis characteristic of infancy and childhood. This sign consists in a transmission downward below the normal limits, of the bronchophony heard on auscultation at the nape of the neck. The spoken voice heard on auscultation over the cervical vertebrae is of a bronchial character. D'Espine pointed out that normally this bronchophony does not extend below the seventh cervical vertebral spine. When there is enlargement of the lymphnodes about the bifurcation of the

trachea and primary bronchi, this bronchophony is heard over the upper dorsal vertebrae. This boundary as described by d'Espine holds for older children, and in them any bronchophony over the upper dorsal vertebrae points towards bronchial lymphnode enlargement. In infants under two years of age, the limit of normal bronchophony must be placed somewhat lower. In a series of cases at the Infants' Hospital coming to autopsy, several have been observed in which bronchophony extended down as far as the third dorsal vertebra, which did not show enlargement of the bronchial lymphnodes. On the other hand, no case in which bronchophony was found below

FIG. 169



Chronic tuberculosis
Showing caseation of the peribronchial lymph nodes

the third dorsal vertebra failed to show enlargement, and most tuberculous cases showed distinct bronchophony over the fourth, fifth, and sometimes even the sixth spines. In infants, therefore, with bronchophony between the seventh cervical and third dorsal spines, the sign may be considered doubtful. With bronchophony below the third dorsal vertebra, the sign is positive, and points strongly toward enlargement of the bronchial lymphnodes.

The significance of this sign in the diagnosis of chronic tubercu-

losis lies in the fact that tuberculosis is by far the most common cause of bronchial lymphnode enlargement in infants and children.

ROENTGEN RAY.—In many cases, tuberculous enlargement of the bronchial lymphnodes can be detected by examining the chest with the Roentgen rays. It is particularly enlargement of the group of lymphnodes which are found along the course of the primary bronchi which is shown in the X-ray plates. Enlargement of the group near the bifurcation of the trachea is masked by the shadow of the spinal column, and is often not visible in the plates unless the mass is very large, or partly calcified. As the group along the course of the bronchi shows enlargement in the majority of cases, Roentgen examination is often of great diagnostic significance.

DIAGNOSIS.—The diagnosis of tuberculosis in infancy and childhood is usually not made during the chronic primary stage. Most of the signs and symptoms looked for in tuberculosis are due to extension of the infection to form secondary lesions. In many infants and some children, such definite clinical signs eventually develop, and when present, the diagnosis is rendered comparatively easy. The most important diagnostic sign of tuberculosis in infancy is the finding of such definitely recognizable manifestations as tuberculous bronchopneumonia, meningitis, cervical adenitis, peritonitis, or pleurisy.

It is unfortunate that the diagnosis of tuberculosis in early life is not often made at an early stage. The tendency toward widespread secondary manifestations is very marked at this age. In infants especially, the secondary manifestations are apt to be very fatal. It is very possible that if the disease were more often recognized at an early stage, the percentage of cases in which extension occurs might be signally reduced.

The diagnosis of tuberculosis in the latent chronic stage depends mainly on three things:

1. The tuberculin reaction.
2. The examination for d'Espine's sign and interscapular dulness.
3. The Roentgen ray examination of the chest.

The general symptoms of chronic tuberculosis in infants and children, such as fever, emaciation, anemia, and cough, are of value only in arousing suspicion, and in calling attention to the need of thorough investigation. Their absence should never be taken as evidence against the possibility of tuberculous infection. Such symptoms as expiratory dyspnea, or the results of pressure on the vena cava or the recurrent laryngeal nerve are significant when present, but are too rare to be of much value in the general diagnosis of the disease. A history of tuberculosis in the family with exposure, is of great value in making a diagnosis.

THE TUBERCULIN REACTION.—In an individual infected with tuberculosis, there are formed certain specific antibodies which are generally distributed throughout the body. These antibodies, when they encounter tubercle bacilli, or a preparation of tubercle bacilli such as tuberculin, cause the liberation of toxic products as a result of the reaction. These products are formed chiefly, first, at the site of the introduction of tuberculin; second, in those areas where there are tuberculous products, or encapsulated bacilli, in which consequently there is an increased quantity of antibody; third, at the site of a previous introduction of tuberculin. The irritation from these toxic products gives rise to local reactions. Furthermore there may be a general reaction, caused by the formation of toxic reaction-products throughout the body, or by the absorption of such products from tuberculous areas. The local reaction in tuberculous areas, and the general reaction only occur when a sufficient quantity of tuberculin is introduced into the general circulation.

The following methods have been employed for eliciting the tuberculin reaction:

1. Subcutaneous Injection.
2. Intra-cutaneous Injection. (Hamburger's Stich-reaction.)
3. Cutaneous Inoculation. (von Pirquet's Test.)
4. Cutaneous Inunction. (Moro's Test.)
5. Conjunctival Application. (Calmette, or Wolff-Eisner Test.)

The subcutaneous test causes a general reaction. It is carried out by giving a subcutaneous injection of a measured dose of Koch's old tuberculin, and taking frequent observations of the temperature. A positive result is shown by a distinct febrile reaction. This test in children is fully as reliable as in older patients, but has very little application in childhood for the following reasons: If no previous test of local reaction has been made, there is no means of estimating the sensitiveness of the patient, and if there happens to be present a large amount of antibody, the introduction of tuberculin into the general circulation may cause an exceedingly severe reaction, with high fever and general toxic symptoms. Furthermore, it can only be employed in cases without fever. It should never be employed without the previous testing of the local reaction. If the local reaction is positive there is no need to test the general reaction. If all local reactions are negative, under ordinary circumstances there is no indication for further testing. In an exceptional case, such as, for example, one in which there are clinical evidences of some lesion, of which the nature is doubtful, and the local reaction is negative, the general reaction can be tried.

Hamburger's intra-cutaneous test is carried out by injecting through a fine needle a measured quantity of tuberculin into the superficial

layers of the skin. The dose is 1 mg. (.1 ccm. of a 1% solution). A positive reaction is shown by the formation of a reddened and somewhat painful induration at the site of the injection, which begins within twenty-four hours and persists for several days. This reaction is, according to the preponderance of evidence, somewhat more sensitive than the von Pirquet test, especially in older children. It is not to be preferred to the von Pirquet test for routine use, because there is always some danger of the appearance of a general febrile reaction. Its chief use is in cases in which the von Pirquet test, even after repetition, is doubtful, or in which, with a negative von Pirquet test, there are other clinical evidences suggesting tuberculosis, but not clearly diagnostic.

The von Pirquet cutaneous test is carried out as follows: The skin of the forearm is washed by rubbing with alcohol or ether, and then two small drops of undiluted tuberculin are applied about 10 cm. apart. The inoculation is made with a scarifier resembling a tiny chisel, which has been sterilized by heating. This is applied first to the skin between the tuberculin drops, and is rotated with a boring motion. The same procedure is then repeated on the skin through the tuberculin drops. The boring is continued sufficiently to remove only the superficial layers of the skin. The blood vessels of the deeper layers should show through, but blood should not be drawn. The middle scarification is made in order to serve as a control. As a precaution against rubbing, the site of the inoculation may be covered with a piece of sterile gauze. A positive reaction is shown by the appearance of reddened areolae about the site of the inoculations, while no reddening is seen about the control. The reaction usually begins within twenty-four hours, reaches its height during the second twenty-four hours, and slowly fades in one or two days. The diameter of the areola varies from five to twenty-five millimeters according to the intensity of the reaction. A negative reaction shows no difference in the appearance of the skin about the control, and the points inoculated. Von Pirquet does not regard the reaction as positive when the areola reaches a diameter of less than five millimeters, even though the points of inoculation look slightly redder than the control. Such a reaction should be considered doubtful, as should also a delayed reaction, in which an areola appears after two or three days. It has been observed that in cases with doubtful reaction, if the test is repeated later, there is often a reaction strong enough to be considered positive. This has been explained on the ground that the introduction even of so small a quantity of tuberculin is sufficient to influence antibody formation in tuberculous individuals. In case negative or doubtful reactions are obtained by the von Pirquet test, it is always advisable to repeat the test in about a week. The

von Pirquet test is the one which, from every consideration, is best adapted to routine use in infants and children.

Moro's inunction test is carried out by rubbing into the skin a preparation of tuberculin made up to fifty per cent strength with anhydrous lanolin. A mass of this about the size of a pea is rubbed for one minute into the skin of the back or abdomen, over an area of about five square centimeters. The reaction is positive when a papular eruption appears over the area in from twelve to forty-eight hours. There is no evidence that this test is any more delicate than the von Pirquet reaction. I have used it once, in a patient who objected to being scratched with a sharp instrument.

Calmette's ophthalmic test is carried out by introducing into the eye a drop of a one per cent tuberculin solution. It is positive when a conjunctivitis appears. It is decidedly not to be recommended for use in children. Severe inflammation of the eye has been known to follow its use.

The Diagnostic Significance of the Tuberculin Reaction.—There is much difference of opinion as to the significance of the tuberculin reaction in infancy and childhood. In general, it is regarded as having its greatest value in early life. It is necessary to distinguish between the significance of a positive reaction, and that of a negative reaction. The tuberculin reaction is undoubtedly specific, and is not seen in individuals who have never had tuberculosis. A positive test is evidence of the existence in the body of specific antibodies against tuberculosis, and therefore that the patient at some time has been infected with tuberculosis. The antibody content is greatest in the years immediately following infection, or in those following a recrudescence of activity, or reinfection. It is for this reason that the reaction is considered to have its greatest value in childhood. Also it is probable that considerable time is required for tubercle bacilli to be entirely eradicated from the body, and that in children once infected, living bacilli are still present, even if they are imprisoned and inactive. In cases showing clinical evidence of some lesion which might be caused either by tuberculosis, or by some other infection, a positive reaction does not necessarily mean that the lesion is tuberculous. It simply means that there is a tuberculous focus somewhere, and increases the probability of any doubtful lesion being tuberculosis.

A positive tuberculin reaction means that there is somewhere in the child a tuberculous focus, containing living bacilli. Consequently, *in the chronic, primary stage of tuberculosis in infancy and childhood, a positive reaction confirms the diagnosis.*

A weak or doubtful reaction suggests that at some time the child has been infected with tuberculosis, but that the process may be

healed. It does not exclude the possibility that bacilli may still be present.

A negative reaction *does not exclude tuberculosis*. The majority of European observers attach greater significance to a negative reaction than seems to be warranted by the experience of others in this country. It is more or less generally accepted, that the reaction is usually absent even in children infected with tuberculosis, under the following conditions:

1. In miliary tuberculosis and tuberculous meningitis.
2. During measles, and possibly during some other acute infections.
3. After treatment with tuberculin.

The negative reaction indicates only that there is not a sufficient quantity of antibody present. I believe that the tuberculous conditions in which the reaction may be negative must be extended beyond the limits of the three given above. I have frequently observed tuberculosis at autopsy in cases which gave a persistently negative reaction, and which did not have acute miliary tuberculosis. It is true that these cases usually had widespread and active tuberculous lesions. I have occasionally, in infants dying from some other cause, found the lesions of the chronic primary stage of tuberculosis at autopsy, after the tuberculin reaction had been negative during life. These cases can be explained on the ground that in weak and feeble babies antibody formation is slow, and that these infants die before sufficient antibody is formed, and before an acute tuberculosis has had time to develop. I should therefore add to the conditions in which the tuberculin reaction may be negative in tuberculous children, the following:

4. In very active stages of secondary tuberculosis.
5. In poorly nourished infants.

In many of these conditions the reaction may be positive or negative. I have seen a positive reaction twenty-four hours before death in a case of acute miliary tuberculosis and tuberculous meningitis, but this is a rare exception. In such cases the reaction is usually negative.

To summarize the significance of the tuberculin reaction in infancy and childhood:

1. A positive reaction confirms the diagnosis of tuberculosis in the chronic latent stage, and is evidence pointing toward the tuberculous nature of a lesion of doubtful character.
2. A weak or doubtful reaction suggests that the child has been infected with tuberculosis, and strengthens the diagnosis of the chronic latent stage when other evidence is present. It suggests that the process may be healed.
3. A negative reaction does not exclude tuberculosis, but is evi-

dence against it, except in acute miliary tuberculosis, in some active form of clinical tuberculosis, in weakly, poorly nourished infants, and in measles and possibly in other acute infections.

D'ESPINE'S SIGN AND INTERSCAPULAR DULNESS.—As tuberculosis is the commonest cause of enlargement of the bronchial lymphnodes in early life, the presence of d'Espine's sign is of great significance in diagnosis. Interscapular dulness or low spinal dulness generally goes with a positive d'Espine's sign.

ROENTGEN-RAY EXAMINATION.—The Roentgen examination, in my experience, gives the most reliable information as to enlargement of the bronchial lymphnodes of any diagnostic method. In many cases the diagnosis of chronic latent tuberculosis based solely on the X-ray examination was later confirmed at autopsy.

The following table gives the frequency of the three important signs of latent tuberculosis in a series of twenty-five cases in which tuberculosis was found at autopsy at the Infants' Hospital:

TABLE 60
Diagnostic Signs of the Chronic Stage of Tuberculosis in Infancy

CASES	D'ESPINE	X-RAY	VON PIRQUET
1.....	o	o	o
2.....	?	?	+
3.....	o	o	+
4.....	?	?	o
5.....	+	+	o
6.....	+	+	o
7.....	o	?	+
8.....	?	+	o
9.....	+	+	+
10.....	+	+	+
11.....	?	+	o
12.....	?	+	+
13.....	+	+	o
14.....	+	+	+
15.....	+	?	o
16.....	+	+	+
17.....	o	o	+
18.....	+	+	o
19.....	?	?	+
20.....	+	+	+
21.....	+	+	+
22.....	+	+	o
23.....	?	+	o
24.....	+	?	+
25.....	+	+	o
Totals.....	{ + ? o 14 7 4	{ + ? o 16 6 3	{ + o 13 12

In general, the presence of any of these three signs is sufficient to warrant a diagnosis of probable chronic tuberculosis. Such a diagnosis is probable enough to warrant treating the case as one of chronic tuberculosis. The presence of either d'Espine's sign or a positive roentgenogram, makes the diagnosis practically certain.

PROGNOSIS.—Tuberculosis is not a self-limited disease, in which, if the patient escapes death, he will eventually recover with certainty. Neither is tuberculosis a chronic infection which eventually leads to certain death. It resembles the ordinary acute infections, in that the child develops a certain power of resistance. It differs from the ordinary acute infections in that this resistance is often not followed by complete destruction of the parasites, but is only sufficient to prevent them from spreading through the body of the host.

FIG. 170



Tuberculosis. Primary stage

The plate shows caseation of the right peribronchial lymphnodes

The danger of death from tuberculosis in infancy and childhood comes from the tendency of the disease to pass beyond the boundaries of the chronic lesions which follow infection, and to invade, more or less widely, the tissues of the child. Death most commonly occurs from some acute or subacute manifestation of the disease. As long as the disease is confined to the primary lesion at the point of entrance and the lymphnodes draining this area, tuberculosis is not the immediate cause of death. In poorly nourished infants who suffer from chronic gastro-intestinal disease, the presence of chronic tuberculosis may be a contributing cause sufficient to turn the scale

against them, but is not in itself the cause of death. Such children also often die from malnutrition without tuberculosis being present.

The prognosis depends mainly on the tendency to severe acute secondary manifestations, and this tendency depends upon the age of the patient. The younger the child, the greater the tendency to severe acute manifestations, such as general miliary tuberculosis, which is certainly fatal, or tuberculous bronchopneumonia, which is dangerous. As the child grows older, the tendency toward general miliary tuberculosis first diminishes, and then the tendency toward tuberculous bronchopneumonia is lessened. In later childhood there

FIG. 171



Tuberculosis. Primary stage

The plate shows caseation of the mediastinal and right peribronchial lymphnodes

still persists a tendency toward secondary manifestations, but these are not of so fatal a character. Tuberculous bronchopneumonia, if it occurs, is less acute and severe; tuberculous peritonitis, pleurisy, cervical adenitis, and bone-joint tuberculosis, become relatively more common.

In any child in the chronic latent stage, there is a possibility of recovery without the process spreading beyond the lymphnodes. In any child thus infected there is at all times throughout childhood

the liability toward an acute fatal attack. In an infant in the first year of life, there is a greater probability of a fatal ending than of recovery. In a child in the eighth year of life, there is strong probability of recovery. Whenever the certainly fatal manifestations—tuberculous meningitis or general miliary tuberculosis—are not present, there is a chance of recovery, no matter how severe the secondary

FIG. 172



Tuberculous bronchopneumonia

The plate shows primary caseation of the bronchial lymphnodes, and secondary infiltration of the lung tissue

manifestations may be. Children show a remarkable capacity of resistance against many of the secondary lesions, and even tuberculous bronchopneumonia may be successfully resisted. Koch has said that a child infected with tuberculosis in the first four years of life is 120 times more liable to death from tuberculous meningitis than is a child between the ages of 10 and 14 years. Hahn followed 69 infants in whom the diagnosis of tuberculosis was made in infancy, with the following results:

TABLE 61

Prognosis in Children Infected With Tuberculosis in the First Two Years. (Hahn)

TIME OF INFECTION	DIED	LIVED
0- 6 months.....	87%	13%
6-12 months.....	74%	26%
1- 2 years.....	61%	39%

In children who survive the tuberculosis of childhood, recovery may be complete, or phthisis may develop in later life. There are no reliable statistics on the liability to late chronic pulmonary tuberculosis.

PROPHYLAXIS.—The chief danger of infection in the child comes from the consumptive adult. The ideal measure in prophylaxis is not to allow the child to live in the same house with anyone known to be infected with tuberculosis, especially an adult consumptive, nor to allow it to visit or receive visits from such an individual. Such strict isolation of the child is not always practical, especially when the tuberculous patient is a parent. Much can be accomplished by insisting that the consumptive parent shall undergo proper sanatorium treatment. When it is impracticable to completely separate the child from a tuberculous parent, the greatest care should be taken to destroy the tubercle bacilli expelled, and to prevent the child from inhaling the spray thrown out in the coughing. All sputum should be carefully collected in proper receptacles and destroyed by germicides or fire. When the tuberculous mother sees the child, it is better for her to visit the child's room than for the child to visit her room, and she should try to avoid coughing in the room if possible. She should never nurse her child, and should avoid kissing it on the mouth. She should have her special eating and drinking dishes, which are boiled after use. Any other tuberculous member of the household, if it cannot be arranged that he or she shall live elsewhere, should be excluded from all contact with the child. Under no circumstances should such a person enter the child's room, and it is better for the child not to come to meals, if a consumptive be present. No wet-nurse, nurse, or other caretaker, should ever be employed, who has ever shown any evidence of tuberculosis. Other children, who have no signs of active tuberculosis, are not a source of danger, but if they have active signs, they should be excluded from contact with healthy children. It is better that children be not allowed to live in a house ever known to have been inhabited by a consumptive. If this cannot be avoided, the whole house should be most carefully cleaned and fumigated with formaldehyde.

While milk infection is rare in comparison with infection by exposure, the danger exists, and is preventable. If possible, only milk of known good conditions of production, from tuberculin tested cows, should be used. Whenever the least doubt exists as to the source of the milk, pasteurization should be employed.

In the case of children known to have been exposed to tuberculous infection, the greatest care should be taken. Parents should be impressed with the fact that care means watchfulness rather than coddling, and that plenty of fresh air is essential in the bringing up

of such children. They should live as much as possible in the open air, and be encouraged to pursue all forms of sport which tend to keep them outdoors. The country is preferable to the city in these cases. If the child is delicate, it should spend the winter and spring in a warm dry climate. The sleeping room should have plenty of fresh air, and the practice of having the patient sleep outdoors on a sleeping porch should be begun if possible after the first summer. The feeding of children with a tuberculous family history should be carefully supervised. They should be guarded as much as possible from exposure to acute contagious infections, such as influenza, measles, and pertussis. In short, every hygienic measure should be employed to favor rugged development, and to fortify them against disease.

TREATMENT.—The treatment of chronic tuberculosis in its primary stage is really prophylactic, in that its chief aim is so to strengthen resistance, that secondary manifestations are prevented. There is no specific treatment which can be successfully directed against the bacilli themselves. Treatment must confine itself to favoring the natural resistance developed by the protective mechanism of the host. The earlier the diagnosis is made, the better are the chances of success.

FRESH-AIR TREATMENT.—The most important therapeutic agent in the treatment of tuberculosis is fresh air. This can best be carried out by having the patient spend practically all its time in the open air. It is not difficult to accustom older children to sleeping outdoors. Whenever it can be arranged, some sort of sleeping porch should be devised. Many houses have some balcony or piazza which can be utilized for this purpose, or even a tent on the roof can be used. During the extreme cold weather of winter, special sleeping garments should be provided, and plenty of bed clothing. On very stormy nights, one or more awnings may be let down. Even in infancy, sleeping out of doors the year round can be carried out successfully. If the disease is first recognized during the winter months, it is not wise to put the infant outdoors at once. The windows of the sleeping apartment can be gradually opened more and more, till finally the infant sleeps in a room with all the windows wide open. But real outdoor sleeping is preferable, and when the disease is recognized during the summer, the practice of sleeping outdoors can easily be continued through the fall into the winter.

The tuberculous child should spend all its time in the open air. The infant should only be brought indoors to have its diapers changed, or to be bathed. Older children should come indoors only to have their meals, or to be bathed, dressed, and undressed, and should be encouraged in every form of play keeping them in the open air. It goes without saying that children of school age must be taken out

of school. In many cases it can be arranged to have a governess give lessons in the open air.

The question usually arises whether a change of climate is advisable in cases of tuberculosis in childhood. It is an open question whether the influence of climate is specific, in the sense that the disease is more favorably combatted when the patient lives in a certain climate, or whether the influence of climate is due to the fact that in warm climates, or in places where everybody is living outdoors, the fresh air treatment can be more thoroughly carried out. It is very probable that much of the benefit of climatic and sanatorium treatment in tuberculosis is due mainly to the thoroughness of the fresh air treatment, and partly to the influence of suggestion. Nevertheless, the winter climate of the Atlantic Coast and the Central States, including the cities of Boston, New York Philadelphia, Cincinnati, St. Louis and Chicago, is not favorable to the outdoor treatment of tuberculosis. It is in general cold and damp, and very variable, rain, snow, extreme cold, or thawing weather, following each other in rapid succession. Under such conditions, the carrying out of the open air treatment is difficult, and requires the most constant care and watchfulness. Even the summer climate of the New England coast has such wide variations of temperature, that care is required. For these reasons, a change of climate is advisable, whenever the circumstances of the family permit. Suitable winter climate may be found in Southern California, Texas, New Mexico, Florida, and the inland parts of South Carolina and Georgia. The Adirondacks and Colorado have good summer climates.

In spite of the advantages of a suitable climate, home treatment is very satisfactory when properly carried out. It is not advisable, merely for the supposed benefit of climate, to take children from good homes, and put them into hotels and boarding houses. The majority of tuberculous patients must be treated at home, and the treatment can be carried out properly in the homes of the well-to-do and middle classes. The results of proper home treatment are quite as good as those of climatic or sanatorium treatment. The advantages of sanatorium treatment are by no means as great in children as in adults. Children need not be sent to a sanatorium except in those cases in which the fresh air treatment cannot be carried out at home, and this condition is only encountered among the poor. Such sanatoria would have to be state institutions. The various tuberculosis clinics which have been organized in the large cities, cooperating with various charities and social service agencies, are becoming most effective in dealing with the problem of tuberculosis among the poor.

DIET.—Careful attention to the diet of tuberculous patients is most important. The successful treatment of tuberculosis is largely

one of nutrition. The feeding of infants should be guided by the principles laid down in the division on Feeding. Many tuberculous infants have great difficulty in digesting cow's milk fat. In such cases I have found that often olive oil can be taken, especially if homogenized. Homogenized olive oil, however, can only be obtained at present in those places where a homogenizer is installed. In older children, the digestive peculiarities of the individual patient must be carefully studied, and a diet prescribed which shall be as nutritious as possible, without passing the limits of digestive capacity. Milk should form the staple article of diet, with cereals, meat, and eggs. Cream, if it can be taken, is fully as useful as cod-liver oil.

MEDICAL TREATMENT.—There is no drug which has any proven specific action against infection with tuberculosis. The remedies most generally advocated in the treatment of tuberculosis, are creosote or guaiacol, and their derivatives, and cod-liver oil. There are numberless clinical reports in favor of these remedies, but, as is well known, such evidence based on clinical observation offers no real proof of value. As in the case of numberless other widely advocated remedies, they may be beneficial, and may not. Creosote and guaiacol, when given by mouth, may do harm by disturbing digestion. Creosote may be given by inhalation. Rachford advocates the use of guaiacol by inunction, combined with lanolin. These remedies are supposed to be lymphatic antiseptics, but there is absolutely no scientific proof of such a theory. If they do good, their value is probably that of general tonics.

Cod-liver oil has certainly no specific action. Its value is found in cases in which nutrition is difficult. In many cases cod-liver oil can be better utilized than other fats. Its use can do no harm. When all fats are not tolerated by the digestive system, cod-liver or some other oil may be given by inunction.

Tonics are sometimes of aid in the treatment of chronic tuberculosis in children. They have no specific action, but may help in promoting nutrition. When the appetite is poor, tincture of nux vomica is indicated, in doses proportioned to the age of the patient, given before meals. Iron is indicated in anemic patients. The compound syrup of the hypophosphites may be prescribed in debilitated nervous patients.

TUBERCULIN TREATMENT.—Of the two forms of specific treatment available in acute infections, serum therapy and vaccine therapy, the former has not given any prospects of success in tuberculosis, but the latter has been widely employed in adult phthisis, with many favorable reports. The therapeutic administration of tuberculin has been as yet too little used in children to enable one to form any conclusion as to its value, and, owing to the nature of the disease,

it will probably be many years before we have definite evidence. It is, however, a specific treatment offering a theoretical prospect of success, and I believe its employment in children has been too much neglected. Properly carried out, it can do no harm, and I believe it should be more widely tried.

The essential feature of the treatment is to begin with very small doses. A dose no larger than one millionth part of a gramme of old tuberculin should be used to begin with ($\frac{1}{1000000}$ milligramme), and the dose gradually increased. The dose may be increased by giving half as much more as the preceding dose at each injection. The injections should be given twice a week. The tuberculin should be given well diluted, and in order to avoid giving too concentrated solutions as the dose is increased, the dilution may be kept constant by the following scheme:

TABLE 62

Scheme for the Therapeutic Use of Tuberculin, in Increasing Doses and Constant Dilution; Injections Twice a Week

Using 1:1,000,000 Solution of Tuberculin

	QUANTITY OF TUBERCULIN SOLUTION		TOTAL QUANTITY OF FLUID INJECTED
1.....	1 ccm.	in	10 ccm.
2.....	1.5 ccm.	in	15 ccm.
3.....	2 ccm.	in	20 ccm.
4.....	3 ccm.	in	30 ccm.
5.....	4.5 ccm.	in	45 ccm.
6.....	7 ccm.	in	70 ccm.

The above scheme is then repeated using a 1:100,000 solution of tuberculin, and is repeated a third time with a 1:10,000 solution. The three stock solutions of tuberculin are made up with sterile normal saline solution, and the same is used as the diluent.

If at any time in the course of the treatment, there should be any febrile reaction, the same dose is given at the next injection, and if fever again appears, tuberculin treatment should be given up. If the above scheme is completed, the patient is taking $\frac{7}{10}$ milligramme at the last dose. The next dose should be 1 milligramme and this, if not followed by fever, should be repeated twice a week for six weeks more.

TREATMENT OF ACUTE MANIFESTATIONS.—When a child with tuberculosis develops fever, it is evidence of increased activity in the chronic lesions, or of extension of the process to form one of the secondary manifestations. It is advisable to put the child to bed, but the fresh air treatment should be continued. If after several weeks, there is no other symptom than fever, and no evidence of any secondary manifestation, and if the vigor of the child has not been impaired, it may be allowed out of bed, and a carefully regulated

amount of exercise may be taken, even though some fever persists. Care should be taken that the child does not get tired.

The symptomatic treatment of the secondary manifestations of tuberculosis is described under the headings of the various organs involved.

ACUTE MILIARY TUBERCULOSIS

SYMPTOMS.—In the majority of cases, when there is acute miliary tuberculosis, the brain is involved in the process, and the symptoms are those of tuberculous meningitis. The symptoms of cerebral involvement so completely dominate the clinical picture presented, that the diagnosis is based on them, and on the results of lumbar puncture. Sometimes, however, the brain is not involved, or is affected too slightly to give meningeal symptoms, but nevertheless there is widespread miliary tuberculosis, involving the lungs, spleen, liver, and often other organs. In such cases the symptoms are often so indefinite that the diagnosis cannot be made. The clinical picture differs somewhat in infants and in older children. It must be remembered that acute miliary tuberculosis is much commoner in infants.

MILIARY TUBERCULOSIS IN INFANTS.—In infancy the symptoms of general miliary tuberculosis are so indefinite, that the diagnosis can seldom be made during life. I have seen infants who showed at autopsy widespread miliary tuberculosis of the lungs, spleen, liver, and kidneys, but who during life had no loss of weight and no fever. This is, however, exceptional. Rapid emaciation is the most frequent symptom of miliary tuberculosis in infants, the clinical picture resembling that of atrophy from gastro-intestinal disturbance. As tuberculous children frequently present symptoms of disturbed digestion, it is usually impossible to tell whether the emaciation is due to a primary nutritional disorder, or is due to miliary tuberculosis.

Fever is often present in the miliary tuberculosis of infancy. The temperature curve is variable, showing nothing characteristic, and nothing by which it can be distinguished from the febrile reactions often seen in gastro-intestinal disorders. Miliary tuberculosis of the lungs presents no physical signs. At any time, the symptoms of some definite secondary manifestation, such as tuberculous meningitis or tuberculous bronchopneumonia, may develop, and clarify the clinical picture.

It is impossible to know how long a course these cases run, because we cannot fix the time at which chronic tuberculosis extended to general miliary involvement.

MILIARY TUBERCULOSIS IN OLDER CHILDREN.—Cases of miliary tuberculosis unaccompanied by tuberculous meningitis are very rare

in older children. When they do occur, the symptoms are also very indefinite. There is rapidly progressive emaciation. The temperature is irregular, and fluctuates from 99° or 100° F. to 104° or 105° F., or even higher. The respirations are often accelerated beyond what can be explained by the fever, and physical signs are markedly absent in the lungs. The pulse is rapid. Certain cases of this class simulate typhoid fever by presenting symptoms of apathy, headache, slightly enlarged spleen, and tympanites.

DIAGNOSIS.—In infancy the diagnosis can rarely be made. When an infant shows emaciation out of proportion to the symptoms of indigestion, especially when accompanied by fever otherwise inexplicable, miliary tuberculosis may be suspected. The suspicion is strengthened if the d'Espine sign is positive, or if Roentgen Ray examination of the chest shows evidence of enlarged bronchial lymph-nodes. The tuberculin reaction in miliary tuberculosis is almost always negative.

In older children, the diagnosis is less difficult in the cases simulating typhoid fever. The fever, though often continuous, is less regular than in typhoid. The spleen is less frequently enlarged, rose spots are absent, and the disease shows no tendency to improve after three or four weeks. The finding of signs of enlarged bronchial lymphnodes, is valuable confirmatory evidence.

PROGNOSIS.—No evidence has ever been found at autopsy that a previous acute miliary tuberculosis had healed. Therefore the prognosis must be considered absolutely fatal. In practice, a fatal prognosis in this disease can never be given, on account of the always existing doubt of the accuracy of the clinical diagnosis. The physician may mention his suspicion of the presence of miliary tuberculosis, and state that it is a fatal disease. If he mentions his suspicion, he should also state that it is only a suspicion, and cannot be more than such, and should encourage hope that his suspicion is wrong.

TREATMENT.—If miliary tuberculosis is present, no treatment will be of any avail, and should be entirely symptomatic and palliative. The cases in infants resembling infantile atrophy must be treated as gastro-intestinal disorders. In the cases resembling typhoid fever, the treatment should be that of typhoid.

SYPHILIS

Syphilis is a chronic infectious disease, caused by the *treponema pallidum* (*spirocheta pallida* of Schaudinn).

ETIOLOGY. THE MICROÖRGANISM.—The specific organism of syphilis was discovered by Schaudinn in 1905, and was called by him the *spirocheta pallida*. It has since been shown to belong in the

class of protozoa, and the name *treponema pallidum* is more strictly correct in biological classification.

The organism is an extremely delicate, corkscrewlike thread of very varying length (4 to 14 μ) and with a varying number of turns (6 to 14). It is motile, and at the end of each spirocheta are extremely minute flagella-like extensions. The organism is present in the lesions of syphilis at all stages. It can be artificially cultivated by special methods. It is pathogenic for man, for the monkey, and for the rabbit.

PREDISPOSITION AND IMMUNITY.—All human beings are susceptible to infection with syphilis. There is no evidence that there is any inherited or constitutional immunity. *Colles' law* has been quoted in favor of the possibility of a passively acquired immunity in the mother of a syphilitic infant. This law is that an infant suffering from congenital syphilis cannot infect its own apparently healthy mother, even though she suckle it, but can infect a nurse. The law is based on the error that a child can inherit syphilis exclusively from the father. The explanation of the immunity so often seen in the apparently healthy mother of a syphilitic infant is that she herself is infected, and has acquired immunity through infection. The primary lesion in women is usually not to be seen, but why the mother of a syphilitic infant is so frequently free from secondary and tertiary manifestations is not known. It is probably connected with the complexity of the immune reactions in syphilis.

Similarly *Profeta's law*, that if a woman suffering from syphilis bears a child that shows no signs of syphilis, the child is immune, is to be explained, not on the ground that a passive immunity is transferred *in utero*, but on the ground that the child is the bearer of a latent infection.

All that is required in order that infection with syphilis shall take place, is that the virus should be transmitted to a proper portal of entry.

Nevertheless, the formation of specific immune bodies plays a very important rôle in syphilis. There is abundant evidence that such antibodies are formed. In the first place there is the fact that in an individual previously infected with syphilis, a fresh cutaneous reinfection usually cannot take place, or if it does occasionally take place, it takes a milder and different form. Furthermore, there are several reactions used in the diagnosis of syphilis, which depend upon antibody formation.

In spite of the immune reaction of the host against the parasite, syphilis is not a self-limited disease. This can only mean that the immune reaction of the host is not able wholly to overcome the parasite. We know very little of the nature of the antibodies. It is, however, highly probable that the clinical reaction of the human

organism infected with syphilis is closely connected with the mode of action of these antibodies. It is the results of the struggle of the defensive mechanism of the host against the biological needs of the parasite which in syphilis, as in many other diseases, appear before our eyes as the picture of a "disease."

The clinical course of syphilis is strongly suggestive of such a struggle. The long incubation period, the localized primary lesion, the widespread generalized secondary manifestations, the increasing tendency to localization of the lesions with each recurrence of manifestations, the circumscribed character of the tertiary lesions, the affinity of the virus at different stages for different tissues—all these peculiarities are suggestive of a contest in which each side has many weapons, and varies its method of attack or defence. It is such a contest which in syphilis, as in tuberculosis, constitutes the picture of a chronic infectious disease.

TRANSMISSION.—Infection with the *treponema pallidum* is always transmitted from a person already infected. Such transmission can take place before birth, during birth, or after birth. When infection occurs before or during birth, the disease is described as *congenital syphilis*. When infection occurs after birth, the disease is described as *acquired syphilis*.

Infection *before birth* is by far the commonest source of syphilis in infancy and childhood. The disease is transmitted always from a syphilitic mother to her offspring; it cannot be transmitted from the father to the ovum by means of the spermatozoa. Belief in transmission from the father to the offspring has formerly been widespread, and many arguments have been brought forward in support of the theory of *syphilis ex patre*. The most important support for this theory is the fact that the mother of a syphilitic infant very frequently shows not the slightest trace of syphilitic manifestations. She is nevertheless immune to infection from her offspring, as Colles' law states. This immunity has been explained in various ways by those who wish to avoid the conclusion that it necessarily means infection of the mother. That immune bodies can pass from the fetus to the mother in such quantity as to produce a lasting passive immunity, or that antigen can pass from the fetus to the mother in such quantity as to produce a lasting active immunity, is contrary to all the evidence provided by modern immunological research. We are forced to the conclusion that *in syphilis, immunity means infection*. Furthermore, the majority of the mothers of syphilitic infants, even though *clinically* free from the disease, nevertheless give evidence of antibodies in the blood which mean infection (Wassermann reaction), and in the maternal portion of the placenta of such mothers spirochetæ can frequently be demonstrated. Finally, in view of our knowledge of the effect of early infection before the

development of the ovum, it is impossible to conceive that an ovum infected from the father could survive. The manifestations of syphilis depend upon a complicated action and reaction between the parasite and the protective mechanism of the host, and the clinical freedom from syphilis in the mothers of syphilitic infants can best be explained on the ground of special conditions in the contest, which are closely connected with the bearing of a child.

The mode of transmission in congenital syphilis is simple enough. The mother is infected before, during, or after conception, and the spirochetæ, which as a result of the infection, are circulating in the blood, enter the placenta and cause specific lesions. The diseased placenta permits passage of the spirochetæ into the circulation of the fetus. Transmission may occur at any stage of pregnancy. The earlier infection takes place, the more marked are the pathological changes produced in the fetus, and the more serious is the outlook for the birth of a living child.

Infection *during birth* is rare, and difficult to establish from clinical manifestations. It can be assumed as a probability when an infant develops a typical primary lesion within a few weeks of birth. With the later development of a primary lesion, acquired syphilis is more probable.

Infection *after birth* takes place in the same way as innocently acquired syphilis in adults. The discharge from a syphilitic lesion must be brought into contact with an abrasion of the skin or mucous membrane, in order that infection shall take place.

CONGENITAL SYPHILIS

PATHOLOGICAL ANATOMY.—The reaction of the tissues of the human body toward the syphilitic virus varies markedly according to the stage of development reached by the human organism. A complete description of the lesions of the disease would occupy more space than can be conveniently allotted to it. I shall endeavor only to give a general picture of the syphilitic tissue reaction. The clinical manifestations of congenital syphilis are for the most part directly due to the pathological changes in the various parts of the body, and those lesions which are of special symptomatic significance will be described under the heading of Symptoms.

The *treponema pallidum* finds its most favorable soil in the fetal organism, because here the tissues have acquired practically no power of resistance against the infection. For this reason, with early infection the fetus usually dies, and the frequency of syphilitic abortion is well known. It occurs most often when the mother is suffering from a fresh and untreated syphilis, and is most common in the fourth and seventh months of pregnancy. The previous history of abortions or still births is of diagnostic significance in syphilis.

When abortion takes place in the first half of pregnancy, the syphilitic changes in the fetus are not very typical. When, however, abortion takes place in the latter half of pregnancy, the syphilitic lesions are pronounced, and it is from such cases that one can best learn the effects of the syphilitic virus upon human tissues, when their powers of resistance are at a minimum. These tissue changes are characteristic and typical of syphilis. When, however, infection occurs late during pregnancy, the child is born alive, and the powers of resistance which are rapidly developed by the tissues continually modify the character of the specific tissue reaction. Nevertheless, the tissue reaction retains its fundamental characteristics, the modifications being the result of a changed local susceptibility and of a more highly developed resisting power.

The fundamental lesions consist in two processes:

1. Diffuse cellular infiltration.
2. Inhibition of development.

Diffuse cellular infiltration is the most characteristic histological manifestation of syphilis. When the infection is acquired early, the cellular infiltration is most likely to involve the visceral organs, in particular the spleen, liver, kidneys, lungs, pancreas, thymus, and bones. The growth of cells has its origin in the interstitial tissues surrounding the smallest blood-vessels, and it is in the perivascular tissue that the spirochetæ are most numerous. In a later stage these changes lead to connective tissue overgrowth with an eventual tendency to contraction.

The inhibition of development characteristic of syphilis is caused by the cell infiltration and hyperplasia of the interstitial connective tissue. There is a corresponding hypoplasia of the parenchyma.

Macroscopically the syphilitic tissue changes show themselves for the most part only in an increased size of the affected organ, particularly of the spleen and liver. In some organs, however, the macroscopic appearances are more characteristic, for example, in the lungs. Here the over-development of interstitial tissue is accompanied by marked fatty degeneration and desquamation of the alveolar epithelium, which can actually fill the alveoli, so that the cut surface of the lung presents macroscopically a peculiar homogeneous yellowish-white appearance—the so-called *white pneumonia*. Another tissue in which the lesion is particularly characteristic is that of the epiphyses of the long bones. These changes are almost constant in the syphilitic fetus, still-born infant, or one dying soon after birth. The lesion is described as the syphilitic osteochondritis or epiphysitis. Macroscopically the epiphyseal line appears to be broader and more yellowish in color than normal. Microscopically the appearances show that calcification, while irregular, is not diminished, but the

formation of true bony tissue is inhibited. The syphilitic infiltration interferes with the formation of the osteoblasts, and the result is a line of worthless granulation tissue. The syphilitic inflammation may so cut off the nutrition of this granulation tissue as to lead to softening and separation of the epiphysis from the diaphysis.

The tissue changes enumerated above are most characteristically found in fetal syphilis, but appear in more or less modified forms throughout the later course of the disease. With increasing powers of resistance, cases of syphilis developing later are less likely to show pronounced changes in the bones and parenchymatous organs. The cellular infiltration of syphilis tends to be localized in certain special tissues, particularly *the skin*. It is curious that in fetal syphilis, the skin is usually wholly unaffected.

SYMPTOMS.—Infants with congenital syphilis are apt to be undersized and of feeble vitality. This is particularly the case in the severer forms of the infection, which, as we have seen, are those which date from a comparatively early period of intra-uterine life. In milder cases the development and vitality of the child are not so notably affected. Syphilitic infants have a tendency to show moderate irregular elevations of temperature. Sooner or later there develops a more or less marked degree of secondary anemia. Furthermore, these infants have a marked tendency to gastro-intestinal and nutritional disturbances, and to infections of the respiratory tract. None of these symptoms are, however, in any way characteristic.

The characteristic signs of congenital syphilis develop soon after birth. In some cases they may be present at birth; more commonly they do not appear for several weeks. Usually they develop before the end of the second month. If an infant reaches three months without developing any characteristic signs, the probability is that it is not syphilitic.

EARLY SIGNS.—There are three important clinical signs of syphilis which may be present at birth. These are:

1. Snuffles.
2. Vesicular eruption on the hands and feet.
3. Enlargement of the spleen.

These three signs are not present in every case of congenital syphilis, and indeed are absent in the majority of cases. They deserve special mention mainly because they are the only important clinical signs which can be seen in the newborn. Their appearance at this time means that infection took place comparatively early in fetal life. They may not appear until a later period, but when present at all, they usually precede the later characteristic cutaneous manifestations.

The *snuffles* are due to the so-called syphilitic rhinitis, which is a

cellular infiltration of the nasal mucous membrane. The nasal passages are narrowed or stopped up, and the result is difficult nasal breathing which manifests itself in a peculiar snuffling sound. The obstruction may be sufficient to interfere with nursing. On examination of the nose all that is seen is a swelling of the mucous membrane, particularly in the posterior part of the nares. In the beginning, secretion is slight or absent, and one never finds the profuse whitish discharge which is characteristic of an ordinary cold. Later there may be a purulent discharge which may be streaked with blood. This rhinitis is by no means seen in all syphilitic infants. When it is present, however, it is seen either at birth or shortly after birth, and rarely appears later than the fourth week. It usually persists for a few weeks and then disappears, but it may be very obstinate, lasting for months. The appearance of snuffles so early in life is apt to strike the attention of the mother, so that a question as to the appearance of this symptom forms an important part of the history in every case of suspected syphilis. It must be remembered, however, that absolute reliance cannot be placed upon the mother's answer to this question, and that the snuffles may have been produced by some cause other than syphilis. When the snuffles are actually observed by the physician, so that he need not depend upon the statement of the mother, they are usually of marked diagnostic significance. The characteristic deformity of the nose, marked flattening of the bridge, which appears at a later period of infancy, is probably to be attributed to an earlier syphilitic rhinitis with its effect upon the development of the nasal bone and cartilage.

The eruption of vesicles upon the hands and feet is the so-called *syphilitic pemphigus* or *pemphigus neonatorum*. The appearance is that of rounded vesicles varying in size from that of a small pea to that of a cherry upon an inflammatory base. The contents of these vesicles are at first serous, but later become cloudy and purulent. The localization of the lesions upon the palms of the hands and soles of the feet, and on the plantar surfaces of the fingers and toes, is wholly characteristic. The syphilitic pemphigus is always a manifestation of an early developing infection. It is not present in the majority of cases of congenital syphilis, and is less common than the syphilitic rhinitis. When present it usually appears at birth. It is always an early sign, and very rarely appears later than the third or fourth week. Occasionally, when an eruption appears late, vesicles are seen on other parts of the body than the hands and feet. The vesicles of syphilitic pemphigus soon become broken, leaving the denuded corium sharply marked out from the epithelial remains at the margin of the lesions. This early eruption is to be sharply distinguished from the later cutaneous manifestations. It is always of very bad prognostic significance.

Enlargement of the spleen, when seen in the newborn, is an almost certain sign of syphilis and indeed is the only sign of visceral syphilis brought over from fetal into extra-uterine life which can be detected on clinical examination. It is by no means always present in newborn syphilitic infants, and even when present is frequently overlooked. Nevertheless, even when not present at birth, it is almost certain to appear at some later period, if only for a short time, so that it may be said to be an almost constant sign of the disease. Its presence in the early weeks of life usually means syphilis; its absence is not markedly against syphilis because it may not be present at the time of the examination.

In addition to the three important signs described above there are a few other manifestations of syphilis which may appear very early, but which are not of so much diagnostic significance. For instance, the liver may be enlarged in the syphilitic newborn. Nevertheless, the liver of the newborn infant is always a large organ, and it is very difficult at this age to be certain of a pathological enlargement. Also there are other pathological conditions which lead to enlargement of the liver in the early weeks of life. Albumin and casts are often found in the urine of syphilitic infants, and may be present in the newborn. Undoubtedly they are due to the effect of fetal syphilis upon the kidneys, but they are not of great diagnostic significance because albuminuria is a common symptom of various diseased conditions in early life. The effects of the syphilitic osteochondritis may sometimes be visible at birth. At this age they usually manifest themselves as a pseudo-paralysis, which is difficult to distinguish from obstetrical paralysis. Most often, however, the bony changes of syphilis do not become visible until a later stage of the disease is reached. Iritis is an occasional manifestation of syphilis in the newborn; when present it is practically pathognomonic. Syphilitic disease of the nervous system, of the organs of special sense (except iritis), and the cutaneous manifestations which are so markedly constant and characteristic in a later stage of the disease, are never seen in the newborn.

Newborn syphilitic infants even at full term are usually underweight. Premature birth is not uncommon, and such infants are usually also below the normal in size and vitality.

CUTANEOUS MANIFESTATIONS.—The typical multiform exanthem of hereditary syphilis is a later manifestation of the disease. It usually appears between the fourth week and the end of the third month. At times the eruption gradually begins to supersede the above mentioned early manifestations. At other times there are none of the early manifestations, and the eruption appears suddenly in children which have seemed healthy in every way at birth.

It is extremely difficult to classify and describe the multiform

cutaneous manifestations of congenital syphilis. In general the syphilides can be divided into two principal groups:

1. Diffuse infiltration.
2. Circumscribed eruption.

1. *The diffuse infiltration of the skin* is simply the appearance in that tissue of the same process of diffuse cellular infiltration which is the chief histological lesion of syphilis in the other organs of the body. The only difference is that the skin is involved somewhat later in the course of the disease. Clinically this tissue-change manifests itself as a thickening and hardening of the skin. Diffuse infiltration of the skin is a special peculiarity of congenital syphilis, and is never seen in the acquired form of the disease.

In rare cases these lesions may involve the skin of the whole body. Usually, however, the lesion is confined to certain particular parts of the body. The regions most commonly affected are the face and the extremities, particularly the hands and feet.

On the face the syphilitic tissue-changes lead to certain clinical signs, which have always been associated with the diagnosis of congenital syphilis. In the first place there is a peculiar yellowish pallor of the face which is difficult to describe. The lips often lose their vermilion border, their color merging into the pallor of the adjacent skin.

Infiltration is particularly marked about the mouth, nose, and eyelids. The process may be so pronounced as to cause the skin to lose all its elasticity. In such cases, wrinkles and fissures appear in those parts where movement of the skin is most active. This is the cause of the well-known *rhagades*, superficial or deep radiating fissures of the lips, which constitute one of the most important of the stigmata of congenital syphilis. When the entire face is involved in diffuse cellular infiltration it presents a peculiar stiff, mask-like appearance.

In some cases the involved areas of the face may show an inflammatory reddening of the skin. The inflammatory process may go further, producing a *crusted eruption* very similar to impetiginous eczema. Such an eruption is seen most frequently about the nose and mouth, but may appear on the forehead or scalp. The crusts are usually easily removed and leave scarcely reddened areas which do not bleed.

Long continued infiltration of the skin naturally interferes with the nutrition of the hair. This is the cause of the *alopecia* which is sometimes seen in congenital syphilis. It may involve the eyebrows, eyelids, and scalp. The syphilitic alopecia usually occupies only the front half of the scalp, in marked contrast to the alopecia of the ordinary restless or rachitic infant.

Localization of the diffuse infiltration in the skin of the soles of the feet and palms of the hands, is very marked. In fact, these regions are a favorite localization of all three types of syphilitic cutaneous lesions—the pemphigus neonatorum, the diffuse cellular infiltration, and the circumscribed eruption. On the palms and soles the clinical appearance is that of a reddened or even livid skin, which has a peculiarly typical, smooth, burnished appearance. This is caused by the extreme tension of the infiltrated skin. If one tries to lift up the skin in a fold, the effort is either unsuccessful, or only the epidermis can be raised. In many cases there is a coarse lamellar desquamation of the horny layer.

At times the cellular infiltration in the skin of the hands and feet leads to a disturbed nutrition of the nails, the syphilitic paronychia.

Diffuse infiltration is frequently seen also in the skin of those parts which are most subjected to irritation from without. It is especially marked on the buttocks and in the groins, especially when those parts are already the seat of intertrigo. The syphilitic process shows itself in an increasing dryness, stiffness, and brownish glistening color of the skin.

2. *The circumscribed cutaneous lesions* of congenital syphilis are somewhat similar to the eruption of the acquired form. Nevertheless, they are almost never general in distribution, but are limited to certain localities. The exanthem of congenital syphilis in no way resembles the syphilitic roseola, which is seen only in the acquired form of the disease.

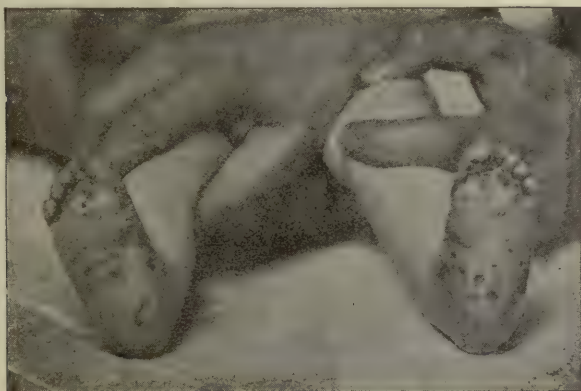
The most typical circumscribed lesion of congenital syphilis is the so-called *maculo-papular syphilide*. This consists in little circular spots varying in size from that of a small pea to that of a ten-cent piece, which in the beginning are rose-red in color, but which later take on a salmon or yellowish-brown color. The lesions appear to be macules, but on close observation can be seen to be very slightly raised, although flat on the surface. In reality they are areas of cellular infiltration of the tissue, with enough inflammatory reaction to cause a hyperemia. These lesions are seen most often on the extremities, particularly on the extensor surfaces and sides of the legs, on the soles of the feet, and on the palms of the hands. The trunk is usually free from the eruption, although in exceptional cases, the entire body may be involved. In the majority of cases the eruption is sparse, and there may be only a few spots on the soles of the feet, on the forehead, on the chin, or in some other region. As a result of irritation, the eruption may become especially profuse about the anus.

The surface of these spots may be cast off by desquamation, leaving behind flat, circular, glistening areas, or else the spots may, without

desquamation, take on a peculiarly characteristic yellowish-brown pigmentation, which eventually disappears.

When the first sign of congenital syphilis is the sudden outbreak of this *maculo-papular syphilide*, it is a favorable prognostic sign. This form of eruption suggests that the human organism has acquired its full reacting power against the syphilitic antigen. Indeed, the more profuse the efflorescence, the better is the outlook. Such cases rarely show signs of visceral changes, such as enlargement of the liver and spleen. When, on the other hand, the circumscribed exanthem is sparse and is preceded by other signs of syphilis, the outlook is not so favorable.

FIG. 173



Syphilitic maculae, ulcers and bullae on the soles of the feet. Male, 2½ months old

At times the circumscribed eruption of congenital syphilis becomes pustular. This is a somewhat different process from the syphilitic pemphigus, which was mentioned as one of the early signs of the disease. It is true that the syphilitic pemphigus may appear for the first time later in the course of the disease, but the eruption is always vesicular from the start, and its presence is always the sign of a severe infection. When the circumscribed eruption of the later stage becomes pustular there is usually a regular progression from macule to papule, and from papule to pustule.

THE MUCOUS MEMBRANES.—In the early manifestations of congenital syphilis which occur in the first three or four months of life, the mucous membranes are affected very infrequently in comparison with the skin. Mucous patches are more characteristic of the relapses which take place later. At times, however, even in early syphilis, mucous patches can be found upon the tongue, lips, or soft palate. Hoarseness or aphonia due to a similar process in the larynx, is seen at times.

THE BONES.—Lesions of the bones, on the other hand, are not uncommon among the early manifestations of congenital syphilis.

The pathological anatomy of the osteochondritis characteristic of fetal syphilis, which is usually present in the newborn, has already been described. In the majority of cases this process does not manifest itself in the newborn by any clinical signs, although at times a very marked development of the process produces the syphilitic pseudo-paralysis of the newborn. If the process advances still further, it leads to changes in the bones which are clinically recognizable. The favorite localizations for this process are the lower ends of the humerus and either the lower end of the femur or the upper end of the tibia. At times the process can be detected in the shoulders, wrists, or in other localities, sometimes all four extremities being involved. These manifestations may be found at any time in the early months of life, and sometimes even later.

FIG. 174



Syphilitic osteo-chondritis

When the process affects the lower end of the humerus, the region of the elbow shows a spindle-shaped swelling, which may be somewhat reddened and hot. The arm hangs in apparent flaccid paralysis with the back of the hand rotated toward the trunk. When the arm is raised and dropped, it falls dead, as if completely flaccid; nevertheless, this is not a true paralysis but only apparent, the nervous system remaining entirely intact. The paralysis is due to one of three possible factors: (1) Extension of the inflammation to the

muscles, causing extreme pain on motion; (2) extension of the infiltration to the muscles, interfering completely with their movement; (3) separation of the diaphysis from the epiphysis.

When other parts of the long bones are affected, such as those about the knees, shoulders, wrists, or ankles, the chief clinical manifestation beside pseudo-paralysis is diffuse bony thickening near the joints. These swellings are often acutely tender. Roentgenograms of the syphilitic osteochondritis give a very characteristic picture. The line of the epiphysis is broadened, irregular, and indented. Next to the diaphysis there is a lighter zone corresponding to the granulation tissue which is formed in this situation. Finally there are increased areas of shadow about the end of the diaphysis corresponding to irregularly formed bony tissue, while the shaft often shows a line of bony thickening along the periosteum.

FIG. 175



Syphilitic dactylitis
Showing the thickening of the periosteum

The syphilitic *dactylitis* is another characteristic bony lesion seen in early life. This process begins very gradually and does not cause either pain or interference with function. The affected phalanx usually shows a marked olive shaped swelling in the region of the middle joint or of the proximal phalanx; occasionally the distal phalanges are also affected. The thickening is entirely in the periosteum, and the joints and soft parts remain unaffected. This process usually begins in early infancy and usually involves more than one phalanx. The appearance closely resembles that of a tuberculous dactylitis, the chief differential point being that the syphilitic process never leads to suppuration or fistula formation.

THE NERVOUS SYSTEM.—The most important manifestation of congenital syphilis in the nervous system is hydrocephalus. This is usually not a very early manifestation, but develops in the third or fourth month, or even later. Syphilitic hydrocephalus can, however, begin to appear right after birth. This manifestation will be more fully considered under diseases of the nervous system.

In addition to hydrocephalus there are various syphilitic infiltrations and scleroses which begin during fetal life, mainly involve the coverings of the brain, and lead to a later idiocy.

THE EYES.—Of the organs of special sense the eyes are the ones most frequently involved in congenital syphilis. The plastic iritis of the newborn has already been mentioned. Later in the disease there can occur a syphilitic retinitis, the specific character of which can be easily recognized by the ophthalmologist. Choroiditis can also occur. On the other hand, the interstitial keratitis, which is so important a sign of congenital syphilis in a later stage, is almost never seen in infancy.

THE VEINS.—A marked dilatation of the veins is often seen in congenital syphilis. This process is most pronounced in the veins of the skull, especially in the temporal region, where the veins may be very tortuous as well as dilated. The process has been associated with hydrocephalus, but is also seen in cases in which no hydrocephalus is present. Dilated tortuous veins are also sometimes seen on other parts of the body. Syphilitic endarteritis is a later manifestation.

THE LYMPHNODES.—A general enlargement of the lymphnodes is an extremely common manifestation of congenital syphilis. The diagnostic value of this sign, however, has been greatly overestimated. The same condition is seen in infancy not only in tuberculosis, but also in a great variety of diseases. Enlargement of the epitrochlear lymphnode is of a little more importance in diagnosis, but even this is by no means pathognomonic of syphilis.

RELAPSES IN INFANCY.—The first manifestations of congenital syphilis, after a variable duration, are apt to disappear even in untreated cases, if the child survives. Before their final disappearance there may be repeated recrudescences, but the manifestations retain their original character. The disappearance of the early symptoms is undoubtedly a manifestation of the defensive reaction of the infant—one phase of the contest between the parasite and the host. In syphilis, however, the disappearance of any set of clinical manifestations does not mean that the disease has been stamped out, and we must expect the parasite to renew its attack at a later date. In the meantime the human organism has, as a result of the survived attack and of its own further development, acquired new powers of defence and a changed method of reaction

against the syphilitic virus. The manifestations now take on a different form, determined by the newly acquired attacking powers of the parasite and defensive powers of the host. When syphilitic manifestations appear after a period in which the infant seemed to be wholly free from symptoms, it is called a relapse. These relapses in congenital syphilis usually occur during infancy or in the first years of childhood, that is, during the first four years of life. Occasionally relapses appear somewhat later, still retaining the manifestations characteristic of infancy. When, however, the renewal of the contest is postponed until about the period of the second dentition, the manifestations are not spoken of as relapses, but as the late syphilis of childhood.

In the relapses of infancy and early childhood the manifestations of the disease are not so general in character, but are more sharply localized. Single lesions, however, are apt to be of greater extent. A variety of eruptions may again appear upon various parts of the skin in this stage of the disease, more or less resembling the maculopapular syphilide. They are apt, however, to appear suddenly, to run a very short course, and to disappear rapidly. The most characteristic manifestations of the relapses of congenital syphilis seen in infancy are:

1. Mucous patches on the mucous membranes.
2. Condylomata on the skin.

1. *Mucous Patches*.—These manifestations are seen most often from the second to the fourth year. Ulcers and mucous patches may be found upon the mucous membrane of the lips, cheeks, tonsils, and soft palate, and on the sides and under surface of the tongue. They are superficial, and of variable size. Infiltration is not marked, but is present to a greater or less degree. Both ulcers and mucous patches have infiltrated edges, but the plaque in this situation rises above the level of the mucous membrane, while the ulcerations are considerably depressed. They are both characteristic of syphilis. Their locality is determined somewhat by the presence of such irritants as sharp teeth pressing against a portion of the tongue. The secretion of all these lesions of the mouth and lips is highly infectious.

2. *The Condylomata* characteristic of this stage are exactly like those seen in acquired syphilis. They are reddened, moist, papular lesions of the skin which vary in size from that of a pea to that of a fifty-cent piece. They grow rapidly in all dimensions. The surface often shows indentations and fissures. The favorite situation of these lesions is around the anus and genitals.

Gummatous lesions may occasionally appear in connection with these early relapses, but are more characteristic of the late syphilis

of childhood. At times a swelling of the testicles is observed in the relapsing stage, which, however, is due to diffuse cellular infiltration rather than to true gumma formation.

THE LATE SYPHILIS OF CHILDHOOD.—The typical lesion of the late manifestation of syphilis in childhood is the gumma. These lesions do not usually appear until the period of the second dentition, and often not until just before puberty. They represent a new reaction of attack and defence between the syphilitic virus and the

FIG. 176



Late manifestations of syphilis. Female, $3\frac{1}{2}$ years old

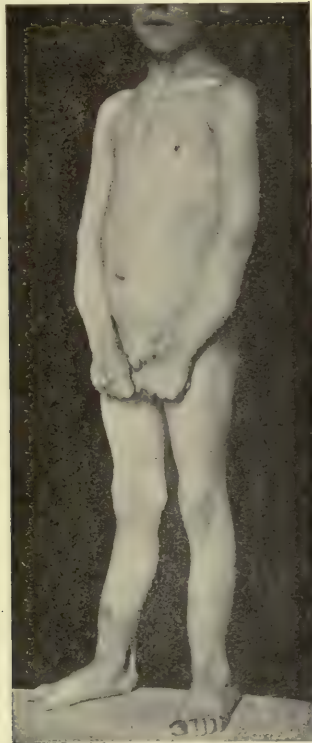
host. Gummatous growths occur most frequently in the bones, skin, mucous membrane, and internal organs. The lesions and symptoms of the syphilitic gummata as they appear in late childhood, often differ in no way from the similar lesions seen in the tertiary stage of acquired syphilis in adults, and will not be described here in detail. There are three particularly important manifestations

of late syphilis in childhood which are quite distinct from gumma formation, and which are sometimes seen in children in whom no evidence of gumma formation is found. These are:

1. Syphilitic periostitis of the tibia.
2. Interstitial keratitis.
3. Hutchinson's teeth.

SYPHILITIC PERIOSTITIS.—In the syphilitic periostitis of the tibia, the shin bone is thickened in its entire length, the over-lying skin being stretched, shiny, and occasionally slightly reddened. The

FIG. 177



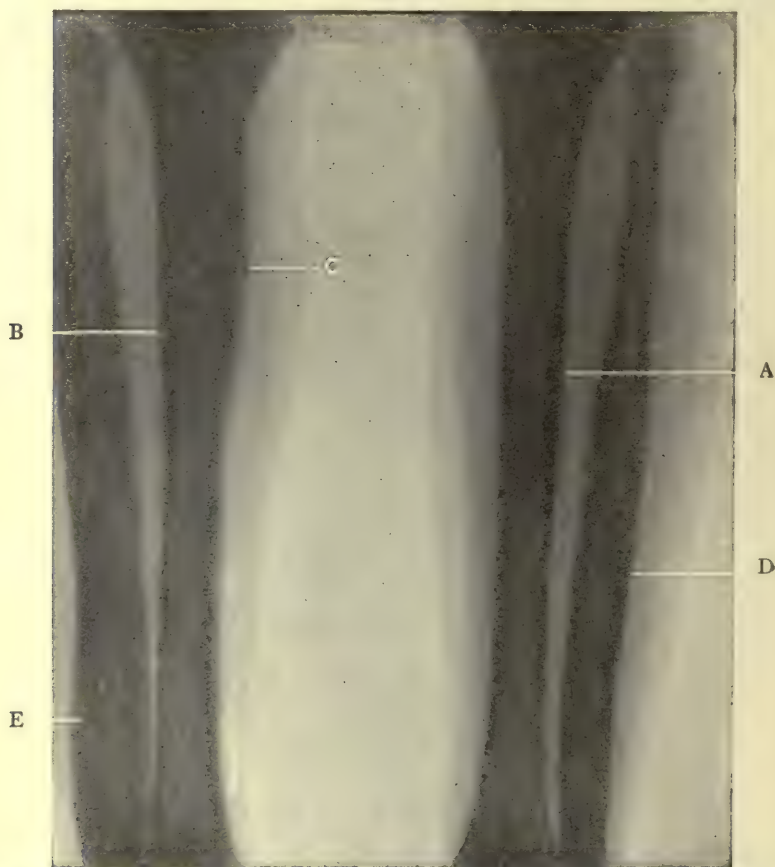
The late manifestations of congenital syphilis in a boy 6 years old, showing periostitis of both radii and both tibiae with an area of softening in the lower third of the right tibia

swelling may or may not be painful to palpation. The impression given is that of a solid spindle-shaped swelling. The edge of the tibia may be lost in the swelling, or may be palpable; in the latter case it is apt to present little roughnesses and indentations.

This inflammatory process in the periosteum may subside or may become gradually ossified. In the latter case, the result is a permanent deformity of the tibia, the so-called sabre leg.

INTERSTITIAL KERATITIS.—In the late form of syphilis a peculiar inflammation of the cornea appears at times. It usually begins with a cloudiness of the substance of the cornea, with ciliary congestion. The entire cornea in this way becomes clouded. The affection is not usually accompanied by pain, and does not show any special congestion of the conjunctivae. It is always symmetrical, although at first it is apt to begin with one eye and later to attack the other.

FIG. 178



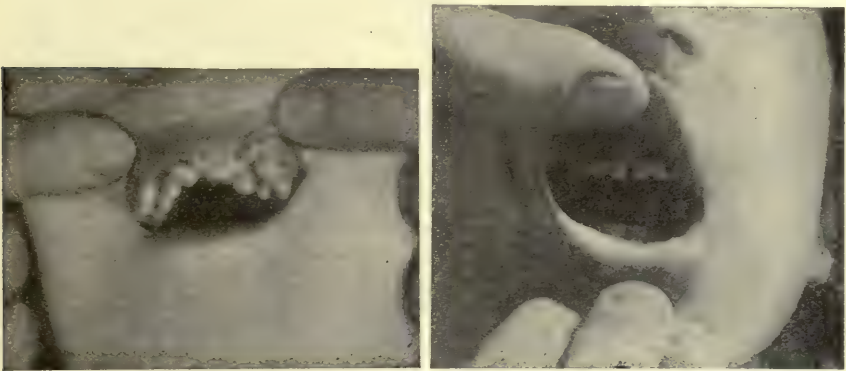
Hereditary syphilis in a boy 8 years old. A, B, C, D, E, represent thickening of periosteal bone of the tibiae and fibulae in the order of the different stages of development

The interval between the two attacks may extend over several years. This disease is called *interstitial keratitis*, and may for a few weeks seriously interfere with the sight. It usually disappears under treatment without leaving any trace of the disease behind it. On the other hand, opacities are sometimes left which interfere with vision. The total duration of the disease varies from six to eighteen

months. Interstitial keratitis occurs most frequently in female subjects, and is most common between the ages of ten and fifteen, although it may occur much earlier, and according to Fournier, may very rarely be met with at birth. Complications may arise in the form of iritis, choroiditis, and retinitis.

HUTCHINSON'S TEETH.—The first set of teeth in infants with congenital syphilis may show the same markings which are characteristic of the second dentition, but usually have nothing characteristic about them; they show a lack of nutrition, a condition which may arise from many other morbid processes.

FIG. 179



Late manifestations of congenital syphilis, showing the typical notched and pegged teeth of the second dentition

The second set of teeth, however, presents certain characteristics. These characteristics are shown especially in the two middle upper incisors, in which the cutting edge of the tooth is worn away, leaving a concave surface. The teeth are also apt to be somewhat far apart, and, as the child grows older, to assume a peg shape. The especial characteristics of syphilitic teeth were first described by Hutchinson. The peculiar shape of the teeth is not always present in syphilis, but when it appears it is very suggestive of the disease. Fournier has called attention to the frequent involvement of the molars. The four cusps may be replaced by yellowish pegs which are free from enamel. These may soon wear down to the surface of the body of the tooth, presenting a smooth crown with yellow center and narrow band of white. Absence of canines and wide separation of the incisors are often caused by congenital syphilis.

In addition to these three signs of the first importance, there are certain other manifestations occasionally seen which are particularly characteristic of late syphilis in childhood.

THE SKULL.—In the late form of congenital syphilis the bones

of the nose are frequently involved, and a flattening of the bridge of the nose is not uncommon. The cranial bones show certain alterations which at times are quite characteristic. The frontal bone may present a prominence on either side, which, with a depression more or less deep between the prominences, causes such a peculiar conformation of the head as to be almost characteristic of syphilis. In addition to these frontal prominences, at times there is a prominence of the center of the frontal bone, which, with the apparent flattening on either side, causes a peculiar shape simulating the keel of a ship. Sometimes protuberances similar to those which have been described of the frontal bone may appear on the parietal bones. When they are bilateral the sagittal suture appears as a depressed sulcus between them, and this deformity of the skull, from its resemblance to the shape of the nates, has been designated by Parrot as the *natiform* skull.

BACKWARD DEVELOPMENT.—An interference with the growth of children who are affected by these various osseous lesions of syphilis is not uncommon. There is frequently a lack of development, which shows itself usually in a failure of the individual to attain the ordinary height. The mental development is retarded, the children often appearing to be a number of years younger than they really are. This condition Fournier has designated as *infantilism*.

THE NAILS.—The *onychia* which occurs as one of the earlier manifestations of congenital syphilis has been described. In the late form of syphilis another form of onychia is met with, characterized by a swelling at the base or the side of the nail, which becomes thickened, fissured, and brittle, with more or less deformity of the phalanx.

THE EAR.—Disturbances of hearing may occur in syphilis from a number of causes, especially from secondary disease of the pharynx. An especial form of *deafness*, however, without any special lesions to explain it, occurs in the syphilis of childhood, is usually intractable to treatment, and persists in later life. Extensive gummatous ulcerations may occur in the *nose* and *pharynx* in the latter part of childhood.

NERVOUS SYSTEM.—Syphilis of the nervous system may be congenital or acquired, involving either the brain or the cord. It is very rare in children. It may occur as a diffuse inflammation of the meninges, as localized gummata, or as an endarteritis. Syphilitic meningitis and endarteritis present essentially the same symptoms as in adults. The brain may be atrophied, showing flattening of the convolutions and distension of the ventricles with fluid. Gummata of the brain or cord present no symptoms in themselves to distinguish them from other cerebral tumors. The lesions in the cord are, however, apt to be widely distributed, involving the cervical, dorsal, and

lumbar regions, with preservation of some of the functions and complete loss of others. The rapid diminution of some symptoms and the persistence of others are characteristic. The presence of syphilis elsewhere and the marked improvement under antisypilitic treatment are important points in the diagnosis. Syphilitic endarteritis and multiple gummata of the base have been observed in infants as early as fifteen months.

DIAGNOSIS. CLINICAL.—The clinical diagnosis of congenital syphilis depends upon the recognition of pathognomonic signs of the disease. In cases in which such signs are clearly evident, the diagnosis is not difficult. Unfortunately all the manifestations of congenital syphilis are not pathognomonic, and the signs observed by the physician at any time may be of doubtful significance. Again, marked signs of the disease may not be present at the time when the case comes under observation, and the history obtained from a child's parents is never wholly reliable as a means of diagnosis. Nevertheless, in all infants who are undersized, who lack vitality, or who have any trouble with nutrition, a painstaking search should be made for all the manifestations of congenital syphilis.

If the syphilitic rhinitis with its snuffles actually comes under the observation of the physician in the early weeks of life, it can usually be distinguished from the snuffles of adenoids or a common cold. A history of snuffles is suspicious, but by no means diagnostic. Typical pemphigus neonatorum is pathognomonic. Enlargement of the spleen in the early weeks, while, perhaps, not absolutely diagnostic, is very strongly suspicious; when it occurs later, other causes must be excluded, such as rachitis or leukemia.

The waxy pallor of the face, and the shiny, glistening soles of the feet, which are characteristic of the stage of cellular infiltration of the skin, are strongly suspicious, if not pathognomonic. If in addition, rhagades are present, the diagnosis is certain. When the process on the face has advanced to the formation of a crusted eruption, the diagnosis of syphilis is not so certain.

The maculo-papular syphilide, when typical, is unmistakable. The difficulty comes from the fact that there may be very few lesions, possibly only a single spot upon the forehead or upon one of the extremities. When the circumscribed eruption is not actually observed, and the physician learns of it from the history, its diagnostic value is much less, and the history can only be termed suspicious. When the circumscribed eruption takes a less typical form, as in certain cases with pustular lesions, the case falls into the suspicious category. Various forms of eczema and dermatitis must be considered as possibilities. The previous history as to syphilitic manifestations is of great importance in such cases.

In the latter half of infancy and in early childhood, congenital syphilis is often suspected only from the history. A positive diagnosis can only be made when manifestations characteristic of this stage of the disease are found. The physician should look carefully at the mucous membrane of the mouth, and at the region about the anus and genitals, for both mucous patches and condylomata present such a characteristic appearance, that their presence is usually diagnostic. Care must be taken not to mistake the mucous patches of syphilis for other forms of stomatitis, such as thrush, stomatitis ulcerosa, and stomatitis herpetica. The mucous patches of syphilis differ wholly from these lesions, but their characteristic appearance can only be learned by observation. They are more sharply localized than thrush, and cannot be removed mechanically. They are whiter in color, and less sharply defined than the circular ulcers of stomatitis herpetica, and are more superficial than the lesions of ulcerative stomatitis. The condylomata must be distinguished from localized patches of eczema.

In late syphilis, the appearance of a bilateral periostitis of the tibia, of interstitial keratitis, or of typical Hutchinson's teeth, is diagnostic.

In many cases, although the history may be suspicious, the patient comes under observation at a time when none of the manifestations enumerated above are present. The physician should look carefully for certain of the more persistent stigmata of the disease. Among these are the depressed bridge of the nose—the "saddle nose" of European writers—and the various permanent deformities of the skull. These stigmata, while not absolutely pathognomonic, strengthen the suspicion raised by the history.

There are certain disease manifestations which may be due to syphilis, or to some wholly different cause. Among these are evidences of a chronic lesion of the central nervous system, hydrocephalus, deafness, retinitis, choroiditis, and so forth. The possibility of syphilis should be remembered in all such cases.

LABORATORY DIAGNOSIS: INDICATIONS.—In the diagnosis of syphilis based upon the clinical manifestations of the disease, cases can be arranged into three groups:

1. Those in which the history and physical examination give nothing suspicious.
2. Those in which the clinical diagnosis can be made with certainty from the character and grouping of the signs found on physical examination.
3. Those in which no sign is found which is positively pathognomonic, but which the history and physical examination bring into the suspicious category.

In the first of the three groups further laboratory investigation is unnecessary, and should not be made as a routine measure. In the second group laboratory investigation, while perhaps not absolutely necessary, should nevertheless be made. It will give positive confirmatory evidence of the correctness of the diagnosis, and no purely clinical evidence is ever absolutely certain. If the case is to be treated with mercury only, the laboratory diagnosis, while not absolutely essential, is certainly desirable. But if the case is of such a severe character as to call for treatment with salvarsan, laboratory examination of the blood is positively indicated. Except in a very unusually acute emergency, *no case of congenital syphilis should be treated with salvarsan unless the presence of a positive Wassermann reaction has been established.*

In the third group, the testing of the Wassermann reaction is positively indicated. The diagnosis can only be made with certainty upon the basis of the Wassermann reaction, and certainty of diagnosis is essential in the treatment of congenital syphilis.

THE WASSERMANN REACTION.—The technic of obtaining the blood for the Wassermann reaction in infants has been described in Division II. At least 1 c.c. of serum is required. Sufficient blood to yield this quantity of serum can best be obtained from the longitudinal sinus in infants. In older children the blood can be obtained from the lobe of the ear, or by making a short incision in the heel.

The technic of the Wassermann reaction or complement-fixation test in syphilis is too complicated for ordinary clinical use. It requires a specially equipped laboratory, and a worker thoroughly trained in the use of the test. There are now laboratories in all the large cities of this country sufficient in number and equipment for the performance of all the tests which may be required. When blood is sent to one of these laboratories, reports will be sent back promptly.

DIAGNOSTIC VALUE OF THE WASSERMANN TEST.—According to the figures given by Noguchi, the most distinguished investigator of the Wassermann reaction in this country, a positive test is obtained in congenital syphilis in 96 per cent of cases. It is probable that the few negative tests were obtained in cases examined very early after birth. These figures probably apply to congenital syphilis as manifested in infancy and the early years of childhood. Noguchi gives 63 per cent as an average for late latent syphilis, but this applies to acquired syphilis. In the latter part of childhood congenital syphilis is in a late latent stage. There are no figures on the Wassermann reaction at this stage, but they probably lie between 63 per cent and 96 per cent.

Positive Wassermann tests have been reported in rare instances of diseases other than syphilis. Among these diseases are yaws,

trypanosomiasis, scarlet fever, leprosy, tuberculosis, carcinoma, and diabetes. The reaction in scarlet fever is only present in the acute stage of the disease. I have never seen a positive reaction in the tuberculosis of early life.

The presence of a positive Wassermann reaction in childhood, with the few exceptions noted above, means that the patient is actually infected with the living spirochetæ of syphilis. It is practically constant in manifest cases, persists for years in poorly treated cases, and disappears under proper treatment even in latent cases. The relation of the reaction to the antibodies formed in syphilis will be discussed under Problems and Research.

The view is now generally held that a positive Wassermann reaction means active syphilis. The test is consequently of extreme value not only in diagnosis, but also as a means of estimating the effect of treatment and the need of further treatment. Its use in this connection will be described under Treatment.

THE LUETIN TEST.—Since Noguchi obtained the *treponema pallidum* in pure culture, it has been possible to prepare an antigen for a cutaneous test similar to the von Pirquet reaction in tuberculosis. Noguchi called this the *luetin test*.

In this test 0.07 c.c. (one drop) of the antigen (luetin) is injected with a fine needle just beneath the epidermis, under aseptic precautions. A control injection with a preparation made from the culture media from which the antigen was prepared, is made on the other arm. When the reaction is negative a rosy areola, with slight swelling, may appear in from twenty-four to forty-eight hours, and fades within seventy-two hours. When the reaction is positive a papule develops in twenty-four to forty-eight hours, which is surrounded by a red areola. The papule increases in size for four or five days, after which involution begins, the lesion disappearing in about two weeks. The papule may become pustular. There is also described by Noguchi a "torpid" form of positive reaction, in which the test remains negative at first, and then, after ten days or longer, develops into a pustular form.

The diagnostic significance of the luetin reaction is still under discussion. The highest percentage of positive reactions has been obtained in the tertiary stage of syphilis and in latent syphilis. Negative reactions are the rule in the congenital syphilis of infancy and early childhood. The chief value of the luetin test in early life is as an adjunct to the Wassermann reaction in the diagnosis of latent syphilis in later childhood.

DEMONSTRATION OF SPIROCHETÆ.—When the *treponema pallidum* can be demonstrated in the products or discharge of the superficial lesions of the disease, the diagnosis is positively confirmed. Un-

fortunately this cannot be accomplished in all stages of congenital syphilis. The organism can usually be found in discharging lesions of the skin, and often in the scrapings from condylomata and from lesions of the mucous membranes.

The best stain for routine use is India ink. A drop of the suspected material is placed on a glass slide and mixed evenly with a drop of fluid India ink of the best quality. A thin smear is then made with another slide in the same way that a drop of blood is prepared for staining. The smear is dried in air, and examined at once with an oil-immersion lens. The spirochetæ appear as glistening, silvery, corkscrew-like threads standing out upon a homogeneous black background.

PROGNOSIS.—The prognosis of congenital syphilis depends mainly on three factors:

1. The general condition of the infant.
2. The character of the syphilitic manifestations.
3. The treatment.

In syphilitic infants prematurely born, the prognosis is very unfavorable. When the infants even though born at full term, are notably below the normal in physical development and vitality, the prospects for their survival are bad. Such infants are extremely difficult to nourish, and are liable both to severe nutritional disturbances, and to intercurrent infections, among which bronchopneumonia stands first as a cause of death. The prognosis is most favorable in infants who appear normal at birth, and who develop normally in the earlier weeks of life, showing no syphilitic manifestations until a later period.

Both the general condition of the infant, and the character of the syphilitic manifestations are largely dependent upon the period of fetal life at which infection occurred. This in turn depends to a great extent upon the stage of the disease in the mother. When the mother has a recently acquired or an untreated syphilis, the outlook for the child is much worse than when she has had the disease a long time, or has been treated. It is well known that the tendency to miscarriage or premature birth diminishes in the course of time, or after treatment, and there is a progressive diminution in the severity of the disease in successive infants born at full term.

In the infant, the later the appearance of syphilitic manifestations, the better the prognosis. Infants who show signs of the disease at birth, usually die. The ominous nature of the syphilitic pemphigus has already been mentioned. Infants in whom the signs are mainly those of visceral syphilis, and who never show pronounced cutaneous manifestations, give a very unfavorable prognosis. On the other hand, when the first manifestation of the disease is a pronounced

outbreak of the maculo-papular eruption occurring after the end of the first month, the prognosis is very favorable. Between these two extremes lie cases in which the first manifestation is the diffuse cellular infiltration of the skin, the prognosis depending upon the nutrition and vitality of the particular infant. Cases which come under observation in the relapsing stage characterized by mucous patches and condylomata, are very favorable for treatment. On the other hand, the late syphilis of childhood, while not immediately threatening, is very resistant to treatment.

The earlier treatment is begun, the better are the prospects both as to life, and as to eventual recovery. Much depends upon the manner in which the specific treatment is carried out. It is essential that it be thorough, and that it be continued until the disease is thoroughly stamped out. Much also depends upon the management of the nutritional problem in the individual infant, and upon the care and nursing which it receives.

TREATMENT.—There are three drugs which have a specific action against the *treponema pallidum*. These are *salvarsan*, *mercury*, and *iodide of potassium*. In the congenital syphilis of infancy and early childhood, the choice lies between salvarsan and mercury. The latter drug may with advantage be used as an adjunct to salvarsan, so that the question to be decided by the physician is whether or not salvarsan is to be employed.

The relative advantages of salvarsan and neosalvarsan in adults is still a subject of discussion. Neosalvarsan is easier to prepare for injection, and there is less danger from toxic effects, but it is less powerful than salvarsan in equal dosage. For use in infancy, statistics seem to prove that *neosalvarsan* is *decidedly to be preferred to salvarsan*.

INDICATIONS FOR NEOSALVARSAN.—There is no doubt at present that treatment with neosalvarsan is a much more rapid and effectual method of ridding the human body of syphilis than is treatment with mercury. Nevertheless salvarsan treatment has not been widely recommended in the treatment of congenital syphilis for two reasons: (1) Because of the danger of arsenical poisoning when so powerful a remedy is given to a young infant; (2) because of the technical difficulties attending the administration of the drug. The danger of producing severe toxic symptoms has been largely, though not wholly, removed by the substitution of neosalvarsan for salvarsan, and by proper regulation of the dose. The drug cannot be given by the subcutaneous or intramuscular route on account of its tendency to produce severe local inflammation, and is best given intravenously. The giving of intravenous injections in infancy has been attended by great difficulty on account of the small size of the veins. The

use of the jugular vein involves a somewhat difficult technic. These drawbacks have been wholly obviated by the use of the longitudinal sinus for intravenous injections in infancy. Some authorities have questioned whether this technic is wholly safe in giving neosalvarsan. This question may not be finally settled, but in my experience the procedure has been safe and convenient.

I believe that neosalvarsan should be used in the treatment of all severe cases of congenital syphilis. In early life the *treponema pallidum* flourishes in the visceral organs, where it produces great damage, and this is the cause of the serious prognosis of the disease. A prompt deliverance of the body from the ravages of the invading parasite is particularly indicated in infancy. In all cases in which the general condition of the patient or the particular syphilitic manifestations are of such a character as to bring the prognosis into the serious category, treatment with neosalvarsan should be begun without delay.

The only type of congenital syphilis in which there is any question as to the advisability of salvarsan treatment, is that in which the patients appear normal in the early weeks, the first manifestation of the disease being a comparatively late outbreak of the circumscribed cutaneous eruption. In such cases the prognosis was always favorable under the old mercurial treatment, although the completeness and permanence of the cure as measured by the Wassermann reaction appear to be less than under salvarsan treatment. However, the completeness and permanence of cure under mercurial treatment depends on the thoroughness with which the treatment is carried out. This must enter into consideration. If the circumstances of the patient are such that the physician is in doubt as to whether prolonged mercurial treatment will be thoroughly carried out, he should recommend salvarsan treatment even in these apparently favorable cases. If, on the other hand, the physician can insure thorough mercurial treatment in this type of case, it is wisest not to run even the slight risk which attends salvarsan treatment. The decision as to the treatment in the relapsing stage of the disease also depends on the prospects of thorough mercurial treatment. This stage is particularly favorable to treatment with mercury properly carried out.

In the majority of cases of the late syphilis of childhood, the treatment is with iodide of potassium. Only when some lesion proves obstinately resistant to this treatment, or when there is a lesion in such a situation as to threaten life, is neosalvarsan indicated.

THE DOSE OF NEOSALVARSAN.—Except in the newborn, the routine dose of neosalvarsan for intravenous administration in infancy is 0.1 gramme. In the newborn it is from 0.03 to 0.05 gramme according

to the size and vitality of the infant. In the latter part of infancy and in early childhood it is 0.2 gramme. The administration of neosalvarsan in an infant should be repeated once, in about ten days. Thereafter mercury is used, and the further treatment is guided by the Wassermann reaction.

THE TECHNIC FOR THE ADMINISTRATION OF NEOSALVARSAN IN INFANCY.—Neosalvarsan comes in ampules, and printed instructions for preparing the solution are provided with the drug. Certain modifications have to be made in preparing the small doses used in infancy. The ampules usually contain a quantity of the drug larger than is to be given. All the utensils and solutions used in the preparation of the solution are previously sterilized, and the entire process is carried out under the strictest aseptic precautions. The ampule is taken from a basin of antiseptic solution, broken with a sterile file, and its contents are dissolved in sterile 0.6 per cent sodium chloride solution, by shaking thoroughly in a mixing bottle. The quantity of normal saline solution used is 10 c.c. for each 0.1 gramme of the drug contained in the ampule. After solution of the drug, the extra fluid is poured away, leaving in the mixing bottle the right amount of solution to contain the desired dose of the drug (10 c.c. for 0.1 gramme). Next 1 c.c. of sterile normal sodium hydrate solution for each 0.1 gramme of the drug is added, the mixture is again shaken until perfectly clear, and then enough of the sodium chloride solution is added to make up the total fluid which is to be given. It is advisable to give the drug well diluted, but there is a limit to the amount of fluid which can safely be injected into the veins of an infant. We have determined at the Infants' Hospital that the maximum amount of fluid which it is safe to give by intravenous injection is one-quarter of the total volume of blood in the infant. Estimating the volume of blood as about one-fifteenth of the body weight, the maximum amount of fluid given intravenously is one-sixtieth of the body weight. In giving neosalvarsan we usually use this maximum, because the neosalvarsan should be diluted as much as possible, in order to avoid the danger of irritation of the tissues if a little leaks out of the vein.

The solution of neosalvarsan prepared in this way must be used *immediately*. It is at once placed in the sterile syringe, and injected into the jugular vein or longitudinal sinus. The technic of intravenous injections through the anterior fontanelle has been thoroughly described in Division II.

TREATMENT WITH MERCURY.—This is used as a substitute for treatment with salvarsan in the milder type of case described above, and as supplementary treatment after salvarsan. The drug is given

to infants by inunction and by the mouth. In the great majority of cases, inunction is the preferable method. I usually order a mixture of mercurial ointment and vaselin in equal parts. Of this a quantity the size of a pea, which contains about gr. x of mercurial ointment, is rubbed daily into the skin. The place of inunction should be changed from day to day. The best localities are the palms, soles, axillae, and inner aspect of the thighs.

The only objection to inunctions is when the family is to be kept in ignorance of the treatment. In such cases the gray powder may be given by mouth in doses of gr. $\frac{1}{2}$ four times a day. Other preparations of mercury offer no advantages in early life.

FIG. 180



Intravenous injection in infancy
Injection of Salvarsan into the longitudinal sinus of a syphilitic infant
A—— L—— before treatment

Mercurial treatment should be continued until the Wassermann reaction becomes negative. It should never be used continuously for a long period, but with occasional periods of about a week of intermission.

TREATMENT WITH IODIDE OF POTASSIUM.—This is used in the later stage of the disease, or when any gummatous lesions are present. The drug is well borne by children. The usual dose for older children is from one to two drachms daily, divided into three doses. In infants the daily amount is from fifteen to twenty grains.

EFFECTS OF TREATMENT.—Experience has shown that the specific treatment of congenital syphilis manifests its effect upon the clinical symptoms of the disease more rapidly and promptly than upon the Wassermann reaction. The clinical symptoms are, however, no good guide as to the completeness and permanence of the effect produced by medication. The Wassermann reaction, on the other hand, is the most reliable measure of the effects of treatment which we have. Experience has shown that the disappearance of a positive Wassermann reaction takes place more quickly after treatment with salvarsan than after treatment with mercury. With salvarsan treatment, the reaction becomes negative in from two to four weeks in most cases, but a positive reaction occasionally persists much longer. The Wassermann reaction should be repeated after long lapses in treatment for certainty of results.

The persistence of a positive reaction after four weeks is an indication for further treatment. In most cases in early life, this further treatment should be carried out with mercury, and should be continued until the reaction becomes negative.

GENERAL AND SYMPTOMATIC TREATMENT.—The feeding and nursing of an infant with congenital syphilis requires the same care as is used in any chronic disease affecting nutrition. It must be remembered that a syphilitic infant in a household may be the source of acquired syphilis in others. Many of the lesions of the disease are highly infectious, particularly the lesions of the mucous membranes. The greatest precautions should be taken to prevent the occurrence of a contact infection. The chief danger to others comes from kissing, and from the use of feeding utensils which have become infected. Rubber gloves, which can be easily disinfected, should be used in the handling of a syphilitic patient. The child should have its own nipples and utensils. Everything which comes in contact with the child should be carefully disinfected.

The anemia of syphilis is apt to be persistent, even after treatment has been begun, especially with mercurial treatment. Under such circumstances iron is indicated. Cod liver oil is useful in some cases with severe malnutrition.

The local lesions usually disappear rapidly under specific treatment. In some cases they are so persistent as to require local treatment. Fissures and ulcers of the mucous membranes are treated with nitrate of silver. Ulcerative lesions of the skin require cleanliness and dusting powders.

PROBLEMS AND RESEARCH.—The principal problem awaiting investigation in syphilis as in most infectious diseases, is that of the nature of the immune reaction of the human organism against the parasite. Syphilis is a disease, the clinical manifestations of

which suggest that the immune reaction is of a particularly complicated nature, and consequently a particularly fascinating problem awaits further research in this direction. Owing to the comparatively recent discovery of the specific microorganism which causes syphilis, and to the still more recent success in growing the organism in pure culture, very little progress has been made up to the present time in the study of the antibodies formed by the host in its contest against the *treponema pallidum*. Almost nothing is known of the antibodies which are undoubtedly formed in syphilis. The varying nature of the clinical manifestations of the disease at different stages is sugges-

FIG. 181



Congenital syphilis

A—— L—— after one injection of salvarsan

tive of a varying virulence on the part of the infecting parasite. Nothing, however, is known as yet about these various factors. The research of the next decade will probably be largely occupied with these problems.

That antibodies are actually formed in syphilis, there can be no doubt. Nevertheless some very interesting light has recently been thrown upon the nature of the Wassermann reaction in syphilis, which apparently shows that the reaction is not dependent upon specific antibodies in the ordinary sense of the term. In the complement-fixation tests which have been used in other infections, it has been shown that the reaction depends upon the fixation of complement to antigen by means of a specific complement-binding anti-

body. It was originally supposed that the complement-fixation reaction in syphilis was produced in the same way. In other infections, however, pure cultures of the antigen were obtainable, whereas at first in syphilis the antigen was prepared from tissue which contained a large number of spirochetæ. It was later shown that it is not the spirochetæ in this tissue preparation which constitutes the antigen, but certain non-specific substances in the extract of syphilitic tissue. When it was found that pure lipoids could be substituted for extracts of syphilitic organs and still be equally effective as antigen in the Wassermann reaction, serious doubt was thrown upon the view that the complement-binding substance in syphilis is a specific antibody. After Noguchi obtained the *treponema pallidum* in pure culture, he was able to prove that the Wassermann reaction does not depend upon specific antibodies as do other complement-fixation reactions. This was accomplished by using an antigen prepared from pure cultures of the organism. When animals were immunized by injections of killed cultures, an immune serum was obtained which gave a complement-fixation reaction with the antigen made from pure cultures of spirochetæ, but gave no reaction with the lipid antigen of the Wassermann test. On the other hand, serum from animals with experimental syphilitic orchitis gave positive reactions with lipid antigen, but not with that made from spirochetæ. The only conclusion which can be drawn from these experiments is that the Wassermann test is a special reaction having for its antigen a substance entirely separate from that contained in the specific organism causing the disease.

This fact explains certain other peculiar features of the Wassermann reaction. Most complement-fixation reactions are found to be present and to persist after recovery from the disease, whereas the Wassermann test becomes less marked or negative as the patient recovers. It has been found that the reaction with the antigen of spirochetæ becomes more marked in patients who had recovered from syphilis, in this way being analogous to other complement-fixation reactions such as that obtained in typhoid fever.

The luetin reaction probably depends upon specific antibodies. It is found most frequently in tertiary and latent syphilis, in fact, in just the cases where the Wassermann reaction gives the lowest number of positive tests.

ACQUIRED SYPHILIS

While the congenital is by far the commonest form of syphilis encountered in early life, acquired syphilis is seen at times. It is possible that in some cases in which the manifestations are first seen in late childhood, and are attributed to an overlooked congenital syphilis, they may really be due to the acquired form.

TRANSMISSION.—Syphilis may be acquired from the mother who contracts the disease subsequently to the birth of the child. Infection may take place by nursing, by kissing, or by some other form of physical contact. The disease may be contracted in the same way from wet-nurses. Also, a syphilitic child may transmit the disease to one who is healthy, both by kissing, or other form of physical contact, and indirectly by means of infected utensils such as bottles, cups, spoons, clothing, and so forth. In former days when human virus was used in smallpox vaccination, syphilis was frequently transmitted in this way, but since the general introduction of bovine virus, the disease has almost never been acquired by vaccination. There have been cases in which the disease was transmitted in the rite of circumcision, from the mouth, or from the instruments of the operator.

SYMPTOMS.—The symptoms of acquired syphilis in children differ in no way from those of the same disease in adults, and will not be described here in detail.

DIAGNOSIS.—The recognition of the disease as belonging to the acquired form depends mainly upon the finding of a primary lesion at the point of inoculation. While in some cases the secondary lesions may resemble those of congenital syphilis, the diffuse cellular infiltration of the skin is never seen in the acquired form of the disease.

PROGNOSIS.—As compared with the congenital form of syphilis, the acquired form is much milder and more favorable.

TREATMENT.—The treatment of acquired syphilis is the same as that of the congenital form of the disease.

DIVISION VIII

DISEASES OF THE LARYNX, LUNGS, AND PLEURA

I. DISEASES OF THE LARYNX

The larynx in infants and children is subject to very much the same diseases as in adults. Congenital malformations are uncommon, the so-called congenital laryngeal stridor representing a condition of backward development. The chief etiological factors are infection, new growths, trauma, and functional disturbance from disease in other parts of the body.

It is not so much in etiology, as in symptomatology, that the diseases of the larynx present markedly characteristic features in early life. There are two causes for the peculiarities of laryngeal disease in young children: The first is the relatively small size of the larynx, particularly in infancy. The narrow opening of the glottis causes most forms of laryngeal disease occurring at an early age to present very much more marked symptoms of obstruction to the respiration than are seen at a later age. The second factor modifying the symptomatology of laryngeal disease in childhood is the great reflex irritability of the nervous system in young children. This reflex irritability is expressed in the larynx by a tendency toward muscular spasm, which also causes obstructive symptoms.

The chief laryngeal symptom is consequently obstruction, which may be caused not only by disease in the larynx itself, but by disease elsewhere affecting the larynx reflexly. The chief diseases in which laryngeal obstruction is seen are the following, in the order of frequency:

1. Acute Laryngitis.
2. Laryngeal Diphtheria.
3. Foreign Bodies.
4. New Growths.
5. Spasmophilia.
6. Congenital Laryngeal Stridor.
7. Acute Infection near the Larynx.

ACUTE LARYNGITIS

(Common Croup; False Croup; Spasmodic Croup.)

This is a condition characterized by catarrhal swelling of the mucous membrane of the larynx, and by a tendency to muscular spasm of the glottis. On account of the frequency of the paroxysmal laryngeal dyspnea, the disease, particularly as seen in infants and young children, is usually spoken of as croup, false croup, or spasmodic croup, as distinguished from laryngeal diphtheria which is called membranous croup, or true croup.

ETIOLOGY.—The disease may be primary in the larynx or may represent an extension from an inflammation in the nose or nasopharynx. The disease is generally considered an infection, and to be most commonly secondary to rhinitis or pharyngitis, or part of the symptom group in measles, influenza, and whooping cough. In my experience primary acute laryngitis is much more common than is generally stated, especially in infants. I believe it to be a question whether bacterial infection is a constant or necessary factor in the production of common croup. The argument in favor of the rôle of infection is based on analogy, as similar catarrhal inflammations in the nose, pharynx, and bronchi, have been shown to be bacterial infections. Against infection is the fact that the comparatively few bacterial examinations which have been made in cases of laryngitis have usually been negative.

There are certainly other etiological factors of great importance in laryngitis. Children are particularly liable to the disease, not often before the age of six months, but very often between the ages of six months and three years. The cause of the liability of young children to laryngitis is probably partly their liability to infections of the nose and pharynx, but chiefly the extreme delicacy and sensitiveness of the laryngeal mucous membrane. The first possibility explains the frequency of association of laryngitis with adenoids and hypertrophied tonsils. The second possibility explains the frequency of attacks of laryngitis which are apparently primary. Certain children are particularly liable to recurrent attacks of laryngitis which can only be explained on the ground of a constitutional predisposition. Such a predisposition, causing extreme susceptibility of the laryngeal mucous membrane, may in some cases be hereditary; in other cases it may be due to anemia, rachitis, chronic tuberculosis or to more obscure nutritional disturbance. The predisposition may not involve the mucous membrane itself, but the nervous system, increasing the tendency to muscular spasm from slight cause.

Another factor is irritation from external causes acting on the mucous membrane of the larynx. It is certain that exposure to

cold, damp, raw, or dusty winds will frequently precipitate an attack, and that such exposure is particularly associated with primary cases. In susceptible children a sudden fall of temperature will often cause an attack of croup. I have seen infants develop laryngitis almost immediately upon being subjected to the cold air treatment for pneumonia. According to the commonly accepted theory of infection being a constant factor in laryngitis, irritation from cold, dampness, or dust, irritates the delicate and susceptible mucous membrane, and makes it more liable to infection. In my opinion, however, it is possible that a mild degree of catarrhal inflammation may be produced in susceptible cases by the direct action of the mechanical or thermal irritant, without actual infection. This may account particularly for many recurrent primary attacks.

I believe it is probable that while infection plays a part in many cases, particularly in those associated with infections of the nose and pharynx, and in those cases in older children characterized by swelling of the mucous membrane rather than by muscular spasm, it may not play a part in many primary cases of spasmodic croup in infants.

SYMPTOMS.—Two distinct symptom complexes are seen. In one, occurring usually in children between six months and five years, spasm of the glottis causes the chief symptoms. In the other, usually seen in older children, but occasionally seen in infancy, the chief symptoms are caused by catarrhal swelling of the mucous membrane.

SPASMODIC CROUP.—The chief symptoms are hoarseness, cough, and paroxysmal inspiratory dyspnea. The attack may occur in the course of a rhinitis or pharyngitis, or may develop as a primary laryngitis. Some hoarseness and cough may precede the actual attack for several days, without any more serious manifestations, and if the child is kept in an equable temperature, the attack may pass off. In some cases, the attack may occur without any preceding laryngeal symptoms.

The child is ordinarily as well as usual in the morning. Towards the latter part of the day, the voice becomes hoarse, and a hollow barking cough is heard, at first neither frequent nor severe. During the night the cough becomes more frequent and severe, and inspiratory dyspnea develops, which in mild cases may not be severe enough to wake the child. Many cases are of this mild character, showing only hoarseness, croupy cough and general discomfort. In more severe cases, the child wakes, and may spring up in bed and clutch at its throat as if frightened. The dyspnea becomes orthopnea, the face is congested, and there may be slight cyanosis of the lips and finger tips. The cough is loud, hoarse, rasping and metallic. There is a loud stridor with each inspiration, as the air is drawn through

the narrow glottis, which may often be heard in the hall as soon as the physician enters the house; I have heard it through the telephone. The breathing is usually slow and labored, with marked contraction of the accessory muscles of respiration, movement of the *alae nasi*, and marked retraction of the suprasternal, supraclavicular, and intercostal spaces, and of the epigastrium. The attack often causes great anxiety, and sometimes even panic, on the part of the child's mother and other members of the household, as suffocation often seems imminent. This reacts on the child, as any excitement increases the spasm.

The temperature is usually slightly elevated, rarely over 102° F; it may be normal. Usually within a half hour there is some lessening of the severity of the symptoms and the attack slowly subsides in from one to three hours, although considerable dyspnea may persist for many hours. After the attack the child is exhausted, and wet with perspiration, and usually falls asleep until morning. Only rarely is there more than one attack in a night. In the morning the child wakes up apparently as well as usual, and wants to get up and play. It continues well during the day except for cough and slight hoarseness. The attack is usually repeated with equal severity on the second night, and sometimes, in much milder form, on the third night. Croup rarely persists for more than three nights. In a few days the cough loses its croupy character, the hoarseness disappears, and recovery occurs.

ACUTE CATARRHAL LARYNGITIS.—This clinical form is seen more often in older children than in infants, and in most cases constitutes part of an infection involving the upper air passages. There is no spasm of the glottis. In mild cases there is hoarseness, which may amount to loss of voice, and a hard cough, which is usually worse at night. There may be some pain and soreness in the region of the larynx. There is usually no fever, except sometimes during the first twenty-four hours, and no constitutional disturbance. The disease runs a course varying from a few days to two weeks. In many children relapses are common.

Severe cases may develop from mild ones, or may be severe from the start. The voice is hoarse and metallic. The cough is severe and almost constant, and is hoarse, dry, barking, and often painful. There is often inspiratory stridor, and some dyspnea, which at times may become severe and paroxysmal. Dyspnea may at times increase progressively, suggesting laryngeal diphtheria. Fever and constitutional symptoms are usually present. The temperature usually varies from 101° to 103°, but may rise higher. The severe symptoms persist for two or three days, after which improvement begins, and the case then runs the course of the mild type. Very severe cases have been known which ended fatally from laryngeal

obstruction. Sometimes the inflammation extends downward, causing bronchitis or bronchopneumonia.

DIAGNOSIS.—Acute laryngitis is to be distinguished from laryngeal diphtheria, from foreign body in the larynx, and from laryngismus stridulus.

Laryngeal Diphtheria.—The essential features of laryngeal diphtheria are a gradual onset, steady progressive increase in the dyspnea, and usually complete loss of voice. The presence of any membrane upon the tonsils, or in the pharynx, points toward diphtheria. The history of cases of diphtheria in the neighborhood may be of aid in diagnosis.

In spasmodic croup, the attack is sudden, usually occurs at night, and is spasmodic in character. The voice is almost never lost. The attack usually soon remits, and disappears the next morning. Rarely some dyspnea may persist on the day following the attack, but it is well to treat any such case as diphtheria. The history of previous attacks points toward spasmodic croup.

In the severe form of acute catarrhal laryngitis, with dyspnea, but without spasm, the diagnosis may be more difficult, especially in the first twelve hours. Laryngoscopic examination will clearly differentiate the two conditions, but it is neither practicable nor conclusive in infants. The dyspnea in catarrhal laryngitis is more likely to be paroxysmal, and remittent, and is mainly inspiratory, while in laryngeal diphtheria it is both inspiratory and expiratory, and increases steadily. The voice is usually not wholly lost in catarrhal laryngitis, and the temperature is usually higher than in diphtheria.

In cases in which any doubt exists, it is best to give antitoxin at once. Cultures should always be taken from the pharynx, and if positive, diphtheria of the larynx is certain, but if negative, no conclusions can be drawn.

Foreign Body.—I have seen cases of foreign body in the larynx mistaken for spasmodic croup. The sudden dyspnea occurring with foreign body is not preceded by hoarseness, cough, nor any catarrhal symptoms. The dyspnea does not tend to remit after a few hours, nor to disappear the next day.

Laryngismus Stridulus.—In this condition, which occurs only in infancy, there is no continuous dyspnea with inspiratory stridor, but a sudden complete cessation of respiration, which is followed by one long stridulous inspiration, and then the attack is over. The attack is usually repeated a number of times, by day as well as by night, and is usually accompanied by the signs of peripheral nerve irritability—carpo-pedal spasm, Chvostek's sign, and so forth.

PROGNOSIS.—The prognosis of simple spasmodic croup is

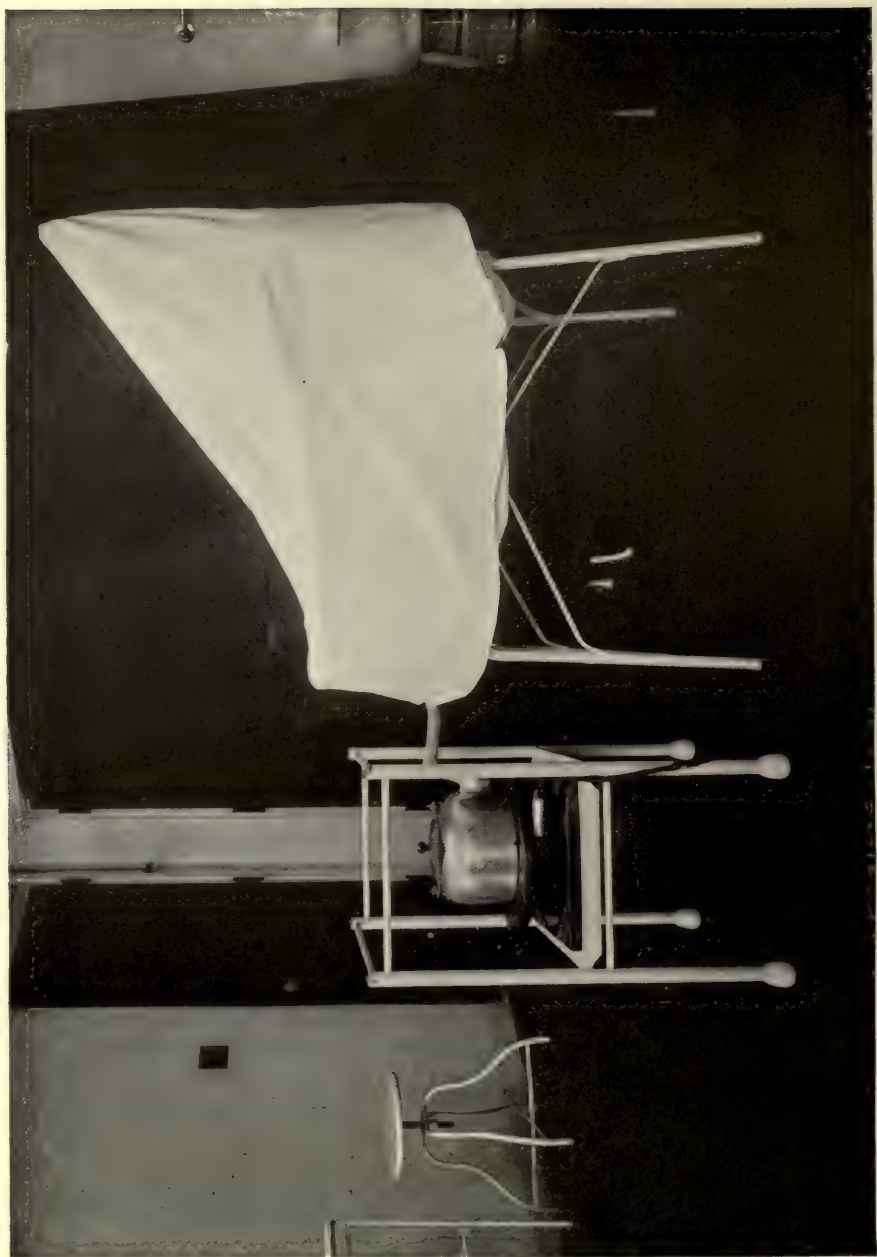


FIG. 182.—Improvised crib tent for steam inhalation

invariably good. The first attack of the disease is very alarming to parents, who should be assured that the condition is never serious. • In mild cases of catarrhal laryngitis without spasm, the prognosis is also good. In severe cases, a more guarded prognosis should be given, especially in cases in which the laryngitis is secondary to measles or scarlet fever. Fatal cases have been known, although the great majority recover. The prognosis is more doubtful in infants, especially if they are weak and debilitated, and more favorable in older children. Another reason for giving a guarded prognosis, is the difficulty of excluding laryngeal diphtheria.

TREATMENT. SPASMODIC CROUP.—During the acute attack, the efforts of the physician should be directed toward causing the laryngeal spasm to relax. This is best accomplished by the influence of warmth, and by causing free secretion from the mucous membrane.

I consider steam inhalation the most effective therapeutic measure in spasmodic croup. Upon arriving at the house, the physician should see that the child is in bed, and warmly covered, with a hot water bottle in the crib. Hot fomentations should be applied to the region of the larynx. The child should be given a drink of warm milk. Free perspiration is accompanied by increased laryngeal secretion. The steam inhalation must next be arranged. Steam diffused in the room is of no use in an acute attack. The crib should be made into a tent by covering it with a sheet. Any apparatus may be used which will furnish steam, and conduct it inside the tent. A croup kettle, several good varieties of which are on the market, is the best method. I have in an emergency used a pipe made of rolled up newspapers, to conduct the steam from the nozzle of an ordinary kettle inside the tent; care must be taken to guard newspaper and sheet from the flame of the lamp. The child should be kept under the sheet until the spasm relaxes, several hours if necessary, the tent being opened occasionally to permit a change of air. I often add compound tincture of benzoin, a teaspoonful to a pint of water, not so much for possible therapeutic effect as because children like the smell.

In a severe case, or if the spasm does not quickly relax, ipecac should be used. Ten minims of the wine, or a teaspoonful of the syrup should be given, and repeated every half hour till the spasm is relaxed, or vomiting is produced. In addition to the ipecac, if the spasm is severe, a dose of five to ten minims of paregoric may be given.

On the following day the child should be kept in a warm room, and guarded against changes of temperature, but need be kept in bed only if there is fever. The bowels should be made to move freely, an enema being given if there is not a thoroughly satisfactory

movement before afternoon. Toward bedtime, as soon as the child begins to cough more, or to become hoarse and croupy, it should be given a steam inhalation. This can be given without the use of the tent, by surrounding a sauce-pan or bowl of boiling water with a cone-shaped newspaper, over which the child is held. It should then be put to bed, in a warm room, which has been previously well-aired, but in which, in cold weather, the windows are not open. A kettle of water should be kept boiling in the room. If the attack recurs, the treatment of the preceding night should be repeated.

In children who are subject to croup, the treatment between attacks is important. In the beginning, they must be guarded against sudden changes of temperature, raw and damp winds, and dust. They should have as much fresh air as possible, without an attack being produced, and experience will show how sensitive they are. They must gradually be accustomed to cold air. The temperature of their baths should be gradually lowered, and they should be sponged daily about the neck and throat with still colder water.

Various drugs have been recommended in the treatment of croup. In the acute attack, in addition to ipecac, antimony is often used in small doses. It is somewhat depressing, and in my experience the combination of antimony and ipecac has no superiority over ipecac alone. In the opinion of many authorities, the recurrence of the attack on the second night can be aborted, or its severity can be lessened, by the use of various so-called antispasmodics. Antipyrin, sodium or potassium bromide, sodium salicylate, and aspirin, in various combinations with ipecac, have been much recommended. The evidence presented in their favor is of the inconclusive clinical variety. My own experience has been chiefly with antipyrin, and I have never been able to convince myself that it has any real value. The bromides are possibly of value, and they would be my first choice.

In very rare cases, the spasm in common croup is so severe, that suffocation is actually threatened. In such a case, intubation is the best measure, and is very effective. If the means of intubation are not at hand, the spasm may be relaxed with a few whiffs of chloroform. Tracheotomy should never be necessary.

CATARRHAL LARYNGITIS WITHOUT SPASM.—Patients should be kept in bed, in a room at a temperature of 70° F., and should have a light fluid diet. The bowels should be freely opened at the beginning of the attack.

The essential feature of the treatment is steam inhalations, given with the tent and croup kettle, as described for croup. Although the steam is the principal therapeutic agent, I usually add a little compound tincture of benzoin in the proportions of a teaspoonful

to a pint of boiling water. In average cases, the steam should be used for fifteen minutes every two hours. In severe cases the steam should be introduced almost continuously.

For the cough, in these cases, a good routine prescription is the following:

Rx	1ST YEAR	2ND YEAR	2-5 YEARS	6-12 YEARS
Paregoric.....	3 ii ss	3 v	3 vii	3 x
Wine of Ipecac.....	3 ss	3 i	3 i ss	3 ii
Sweet Spirits of Nitre.....	3 ii ss	3 v	3 vii	3 x
Water.....ad	3 iv	3 iv	3 iv	3 iv

M. Sig. Teaspoonful every four hours.

If there is much spasmodic dyspnea, ipecac given as in croup, may be used every now and then, till the spasm is relieved.

Hot fomentations may be applied to the region of the larynx. Sometimes a mustard paste, just sufficient to redden the skin, will give relief. Late in the course of the disease, stimulants may be necessary.

In cases with severe dyspnea, such as are sometimes seen in infants and young children, operative interference may be necessary. The difficulty in being sure that the case is one of catarrhal laryngitis only, and not of diphtheria, makes it wise not to allow any case with dyspnea from laryngeal obstruction to advance too far. Even if the physician is sure the process is only one of catarrhal swelling, increasing dyspnea with marked prostration should be the signal for interference. Intubation is the operation to be preferred.

EDEMA OF THE LARYNX

This condition is characterized by an edematous swelling of the submucous cellular tissue of the larynx. The edema may be serous or inflammatory.

ETIOLOGY.—The serous form is a true edema, the fluid accumulating in the tissues being a transudate, not an inflammatory exudate. It is usually part of a general edema occurring in certain diseases characterized by edema, such as nephritis, or cardiac insufficiency. In very rare cases a localized laryngeal edema may be caused by mechanical interference with the circulation from a tumor or enlarged lymph nodes. Serous edema is rare in early life.

In the inflammatory form, the fluid is an inflammatory exudate, with fluid and some cell infiltration similar to the collateral edema seen around acute infections in other parts of the body. It is seen most often in acute infections of the larynx, or of the tissue near the larynx. It may complicate a primary acute laryngitis, or retropharyngeal abscess, or erysipelas or cellulitis of the neck. It may be caused by the irritation of a foreign body in the larynx, or by

mechanical irritation of the larynx, such as from trauma, burns, or irritating gases. It is a rare complication of some of the acute infectious diseases.

The usual location of the edema, in both forms, is in the aryepiglottic folds and epiglottis. More rarely it involves the vocal cords and the interarytenoid fold. The serous form is more apt to be symmetrical than the inflammatory.

SYMPTOMS.—Marked inspiratory dyspnea, with suffocative attacks, is the most important symptom. In the serous form there is usually present edema in other parts of the body, and the signs of the primary disease. In the inflammatory form, there is usually pain and difficulty in swallowing, hoarseness and cough. The symptoms usually develop rapidly, and may lead to fatal obstruction in a few hours. On inspection with the laryngoscope or laryngeal mirror, the edematous tissues may be seen. On introducing the finger, the swollen aryepiglottic folds may easily be felt and recognized.

PROGNOSIS.—The prognosis varies according to the cause and severity in the individual case, and upon the promptness with which treatment is instituted. The milder cases of the serous form usually recover. Severe inflammatory cases tend toward a fatal ending.

TREATMENT.—Ice should be applied externally to the region of the larynx, and pieces of ice may be dissolved in the mouth and swallowed. A specialist should be called whenever possible, as further treatment is operative, and should be carried out by one familiar with such procedures within the larynx. The first step is scarification or multiple puncture. If this fails to bring relief, tracheotomy should be performed. In this condition it is far preferable to intubation, and should be undertaken not as a last resort, but before the patient's condition becomes desperate.

Vigorous treatment of nephritis and cardiac disease should be instituted, when the edema is due to those conditions.

CONGENITAL LARYNGEAL STRIDOR

This is a rare congenital condition of unknown cause. It is probably a congenital anomaly in the formation of the larynx, consisting in a small epiglottis, with the edges so turned back as to bring close together the aryepiglottic folds, with a consequent narrowing of the lumen. Heubner believes the anomaly to consist in a congenital lack of firmness in the laryngeal tissues.

SYMPTOMS.—The characteristic symptom is a crowing stridor, which is purely inspiratory in character, and which begins in the first few days after birth. The stridor is present even during sleep.

At first there is no noticeable dyspnea, but later paroxysms of dyspnea may be seen, which are rarely severe. Inspiratory retraction in the supra-sternal and supra-clavicular regions, and in the epigastrium, is rarely seen. Cyanosis is very rare. Expiration is easy and noiseless at all times. The stridor and dyspnea may grow worse during the first six months, then begin to get better, and will usually have disappeared before the end of the second year.

DIAGNOSIS.—The diagnosis is made mainly on the fact of the appearance of the condition right after birth.

PROGNOSIS.—The prognosis is favorable.

TREATMENT.—No special treatment is required. In infants brought up under favorable hygienic conditions, there is no unfavorable complication to be feared.

FOREIGN BODIES IN THE LARYNX

The aspiration of foreign bodies into the larynx is not uncommon in young children, on account of their habit of putting things into their mouths. Attempts to cough, laugh, or cry, frequently result in the foreign body being drawn into the larynx. The foreign body usually excites such a paroxysm of coughing, that it is expelled. Sometimes, however, it may become impacted in the larynx. In such a case, the glottis may be completely occluded, and death may occur from suffocation. More commonly the foreign body does not produce complete occlusion, but excites a severe acute laryngitis or edema.

SYMPTOMS.—Usually there is a sudden attack of cough and inspiratory dyspnea. Later the dyspnea increases, and hoarseness develops more insidiously. I have seen a case in which there occurred during the night an attack which in every way resembled spasmodic croup. In the morning the obstructive symptoms grew worse rather than better, and the diagnosis was changed to laryngeal diphtheria. An attempt to perform intubation not only failed, but caused acute suffocative symptoms, and a hurried tracheotomy was performed, which was not completed in time to save the child's life. A flat fish-bone, half an inch in diameter, was found in the larynx.

DIAGNOSIS.—Usually the suddenness of the onset of obstructive symptoms, without previous signs of catarrhal inflammation, suggests foreign body. In cases of slower development, the diagnosis may be difficult. Laryngoscopy should be employed whenever possible. Some foreign bodies can be shown in radiograms. The possibility of foreign body should always be remembered.

PROGNOSIS.—This depends upon the ease with which the diagnosis can be made, and with which the foreign body can be removed.

TREATMENT.—The foreign body is removed with forceps, care being taken not to push it deeper.

PAPILLOMA OF THE LARYNX

New growths in the larynx in infants and children are rare. They may be congenital, but these are very uncommon. They may be malignant, such as epithelioma and sarcoma, or benign, such as fibroma, myxoma, and papilloma. Those of the former class are so rare that they need here only to be referred to. Of the latter class fibroma and myxoma are too rare to be more than mentioned. Papilloma, on the other hand, although comparatively rare, is the most common laryngeal growth in early life. They may produce such serious results that it is important to recognize them at once. They may be congenital. Their cause is not known. Papilloma of the larynx in young children is usually multiple.

SYMPTOMS.—The symptoms of this growth appear at about the first, second, or third year. The first symptom that is noticed is hoarseness. This hoarseness, instead of passing off in a few days, as is common when it arises from other affections of the larynx, continues and grows more marked. The next symptom is dyspnea. This appears after an interval of a few months, or may not arise for some years after the first alteration of the voice. The dyspnea first appears at night, when the child is asleep. In the daytime, when the child is awake and running about, it may breathe freely. As the papillomata increase in size, the dyspnea appears in the daytime also, especially when the child makes any exertion. When it is awake and is quiet the breathing may not be noticeably affected, even after the growth has attained a large size. Cough may be present. Usually there is no pain nor difficulty in swallowing.

DIAGNOSIS.—When a child presents these symptoms a careful laryngoscopic examination should be made at once, as in this way only can the diagnosis be verified.

PROGNOSIS.—The prognosis is favorable. Some cases terminate in spontaneous recovery, without operative interference. This, however, will not occur in the majority of cases, and whenever dyspnea has developed, operative treatment should be recommended. Favorable features in the prognosis are that this form of new growth does not become malignant, and that operative treatment is usually effective, owing to the tendency toward eventual spontaneous recovery.

TREATMENT.—The treatment should if possible be placed in the hands of a specialist accustomed to operating on the larynx. The endolaryngeal removal of the tumor is the first operation employed. Pedunculated tumors are easier to remove than those

having a broad base. After removal, recurrence often occurs. If recurrence occurs, or if when the case first presents itself for operation, dyspnea is marked, tracheotomy should be performed. After tracheotomy, the tendency of the papilloma eventually to disappear spontaneously is apparently increased, and can be taken advantage of. It is usually necessary for the child to wear a tracheotomy tube for at least a year.

CHRONIC LARYNGITIS

A chronically congested or catarrhal condition of the larynx is sometimes seen in children, although it is rarer than in adults.

ETIOLOGY.—The causes of chronic laryngitis are the following:

1. Adenoid Growths in the Pharynx.
2. Tuberculosis of the Larynx.
3. Syphilis.
4. New Growths.

SYMPTOMS.—The symptoms are chronic hoarseness and laryngeal cough. In tuberculous laryngitis there is often muco-purulent, and sometimes bloody expectoration, and the hoarseness may amount to aphonia.

DIAGNOSIS.—Diagnosis consists in recognizing the cause of the condition. In the form associated with adenoids, or with hypertrophic rhinitis, laryngeal inspection shows only congestion or slight catarrhal inflammation. In the tuberculous form, laryngoscopy usually reveals tuberculous ulceration, which is rather superficial. In syphilis the laryngoscopic picture is very similar, and the two conditions are to be differentiated by the general features of the two diseases. New growths are easily recognized.

PROGNOSIS.—The prognosis of the form associated with adenoids is very favorable, as removal of the cause is followed by very rapid improvement. The prognosis of tuberculous laryngitis is fairly good in children, as is that of syphilis in the majority of cases, when properly treated.

TREATMENT.—The treatment is that of the cause.

II. DISEASES OF THE LUNGS

The diseases which affect the lungs in children can easily be classified upon an etiologic basis. Of the five principal classes of disease, malformations and new growths are too rare to need description. Diseases of the lungs in classification come under the headings—1. Mechanical Injuries; 2. Functional Disturbances; 3. Infections. The following conditions are seen most frequently:

I. Mechanical:

- Foreign Bodies.
- Bronchiectasis.
- Atelectasis.
- Emphysema.
- Hypostatic Pneumonia.

II. Functional:

- Asthma.
- Recurrent Bronchitis.

III. Infections:

- Bronchitis.
- Pneumonia.
- Abscess.
- Gangrene.

As the infections constitute the most important class, they will be described first.

ACUTE BRONCHITIS

This is an acute infection involving the bronchi, and is a very common affection in infancy and childhood. It is most often seen in infancy, its frequency diminishing steadily after the second year.

ETIOLOGY.—The causes predisposing toward infection of the bronchi are the same as those predisposing toward infection of the upper air passages in general. The following are the principal predisposing causes:

HEREDITARY PREDISPOSITION.—There is some evidence that a constitutional peculiarity may be inherited, which causes an increased sensitiveness of the mucous membrane of the respiratory passages. This only can explain the liability of certain individual children to repeated attacks.

ACQUIRED PREDISPOSITION.—Infection of the respiratory tract is particularly common in children who are coddled too much. They

do not get enough fresh air, as they are kept indoors much of the time, and are not allowed to go out unless the weather is particularly fine, for fear that they may catch cold. They live in overheated rooms, and sleep in rooms with the windows closed, and are habitually over-clothed. These conditions may lead to an abnormal sensitiveness, so that very slight exposures to changes of temperature result in congestion of the bronchial mucous membrane.

CONSTITUTIONAL DISEASE.—Bronchitis is particularly common in children having rachitis, and it is probable that other constitutional diseases with malnutrition act as predisposing causes.

LOCAL DISEASE.—Adenoid vegetations and enlarged tonsils are well-known foci for respiratory tract infection, and are important predisposing causes of bronchitis.

EXPOSURE TO COLD.—This is often the immediate exciting cause of an attack of bronchitis, especially in children made susceptible by faulty hygiene. When a child becomes chilled, there is a certain amount of congestion of the internal vessels, in which those of the bronchial mucous membrane are involved. In the presence of such congestion, the liability to infection is increased. Sitting in draughts, exposure to severe cold without proper clothing, "cooling off" rapidly after profuse perspiration, wetting the feet, throwing off the bed-clothes at night, are all ways in which external chilling may occur. Consequently bronchitis is much more common in cold weather, particularly in the late winter, and early spring.

CONTAGION.—Respiratory tract infection can undoubtedly be conveyed from one individual to another, particularly in acute rhinitis. Any infection of the upper respiratory passages may extend to the bronchi.

IRRITANTS.—In very rare cases bronchitis may be caused by the inhalation of irritants.

THE MICROORGANISMS.—The infection is usually mixed, several varieties of bacteria being concerned. The microorganisms most frequently found associated with bronchitis are the pneumococcus, and the staphylococcus aureus; next in importance is the streptococcus. During epidemics of grippe, and in protracted cases, the influenza bacillus is frequently found.

Bronchitis is most frequently associated with more or less general respiratory tract infection, representing merely a more extensive involvement of the mucous membrane. It may either accompany or follow such conditions as rhinitis, pharyngitis, or laryngitis. It is an almost invariable accompaniment of those specific infections particularly involving the respiratory passages, such as measles and influenza, and is often seen in other acute infections, particularly in pertussis, typhoid fever, and diphtheria.

Bronchitis may be primary, in the sense that the infection is confined to the bronchial mucous membrane only, without evidence of disease elsewhere.

PATHOLOGICAL ANATOMY.—Bronchitis is an inflammation of the mucous membrane of the bronchi, of the kind commonly called “catarrhal,” on account of the profuse secretion of mucus which characterizes the process. The mucous membrane is first congested and swollen, then there is a free secretion of mucus, the exudate containing polynuclear leucocytes and desquamated epithelium. The exudate is more cellular when the smallest bronchioles are involved.

The process is usually bilateral and diffuse. The types of the disease may be classified according to whether the larger or smaller bronchi are involved. There is no etiological foundation for such a subdivision, but there is a certain correspondence between the clinical manifestations and the size of the bronchi most involved, which makes the clinical description clearer under such a classification. We have three subdivisions,—

1. Involvement of the larger bronchi only. This is the ordinary tracheo-bronchitis, most common in older children.

2. Involvement of the medium-sized bronchi. This is the common acute bronchitis of infancy, and is seen in the severe cases of older children.

3. Involvement of the smallest bronchioles. This is the so-called capillary bronchitis, and is only seen in infancy.

It must be remembered that acute bronchitis in the majority of cases represents a more or less general infection of the respiratory tract. Any upper respiratory infection may extend to a bronchitis, and any bronchitis may extend from larger bronchi to smaller, or still deeper to cause bronchopneumonia. The diagnosis of bronchitis, and of the particular form according to the size of the bronchi affected, is important only on account of its prognostic significance and the treatment, which vary with the anatomical and clinical type.

There has been considerable discussion as to whether there is such a condition as capillary bronchitis, based on the question whether the finest bronchioles can be involved without the inflammation extending into the alveoli and causing a bronchopneumonia. The doubt of the possibility of the separate existence of capillary bronchitis is strengthened by the fact that almost invariably when capillary bronchitis is the clinical diagnosis, the autopsy shows bronchopneumonia. The same thing is, however, true of the severe bronchitis of the medium-sized bronchi; cases diagnosed as bronchitis often show bronchopneumonia at autopsy. Any acute bronchitis, especially in an infant, is liable to extend to fatal bronchopneumonia, and this is especially the case when the smallest bronchioles are affected. In

most fatal cases of capillary bronchitis, extension to the alveoli has occurred, and this explains the post-mortem findings. This does not, however, preclude the possibility that in cases which recover, the process may have been confined to the bronchioles without involvement of the alveoli. Without post-mortem proof, however, we could not designate a particular clinical picture as characteristic of capillary bronchitis. Such post-mortem proof has been offered. I have myself seen at autopsy a lung in which all the bronchioles were filled with exudate without any trace of exudate in the alveoli, which were emphysematous. Similar cases have been frequently reported by European writers, the majority of whom regard capillary bronchitis as a separate disease entity, with characteristic clinical manifestations. Probably in most cases of capillary bronchitis which end fatally, bronchopneumonia has supervened, but in those cases clinically suggesting capillary bronchitis, when bronchopneumonia does not supervene, recovery occurs.

SYMPTOMS. ACUTE TRACHEO-BRONCHITIS.—This form is most commonly seen in older children, but occasionally it accounts for mild cases of bronchitis in infants. The onset is usually gradual, and fever may be entirely absent. Sometimes there is a moderate febrile reaction lasting one or two days. Other constitutional symptoms are usually absent, and the patient is not sick enough to go to bed. The first symptoms are cough, and a feeling of soreness or oppression under the sternum. The cough is at first hard, dry, and racking; later it loosens, and there is usually expectoration in children over five years of age. The sputum at first consists of white, frothy mucus, and later becomes yellow. The respiration is not accelerated in older children. There may be loss of appetite, coated tongue, or slight disturbance of digestion.

Infants, when affected by this mild form, usually have moderate fever for a few days. The respiration may be moderately accelerated, and accompanied by a coarse rattling sound in the chest. There is no expectoration.

The physical signs show no modification to percussion, and the vesicular respiratory murmur is normal. In the early stage, coarse, dry, sonorous râles are heard in various parts of both sides of the chest. Later these are replaced by coarse mucous râles. In some cases very few râles are heard, the only sign on auscultation being a few very coarse ronchi, or mucous rattling.

The disease runs a course of from one to two weeks. If children are confined to the house throughout, the disease is liable to become prolonged, a protracted "winter cough" resulting, or to keep recurring. Prolonged or recurrent cases should always give rise to the suspicion of a possible tuberculosis or influenza.

ACUTE BRONCHITIS OF THE MIDDLE TUBES.—This is the form most commonly seen in infants, and is responsible for the severe cases occasionally seen in older children. The onset may be gradual, preceded by symptoms of a cold, or it may be sudden. Fever is present, the temperature usually ranging from 101° F. to 102° F., but occasionally going to 103° or 104° in the first two days. The temperature curve is irregular; after the first two days, the temperature gradually tends to fall. The pulse is slightly accelerated. The respiration is moderately accelerated. The cough is at first dry and teasing, but later becomes looser. Children under five years swallow the sputum. In infants the swallowed sputum often causes digestive disturbance, as evidenced by loss of appetite, bad movements, colic, and sometimes vomiting.

In older children, there is a feeling of tightness under the sternum, and after the cough loosens, profuse expectoration, which is sometimes streaked with blood. Loss of appetite, headache, and a feeling of weakness, are sometimes seen.

Physical examination shows, in the early stage, sibilant and sonorous râles all over the chest. After about twenty-four hours these are replaced by moist râles, both coarse and fine, but not of the finest crepitant variety. The râles are heard all over, but best in the back. The vesicular respiratory murmur is diminished in intensity.

The acute stage of the disease lasts usually about a week. As recovery occurs, the finer râles disappear first. Cough, and some coarse râles are likely to persist for another week, and the cough may persist even longer.

The extension of an acute bronchitis into a bronchopneumonia is shown by three things: 1. Increase in the rapidity of the respiration; 2. The appearance of crepitant râles; 3. Increase in the constitutional disturbance.

CAPILLARY BRONCHITIS.—This condition is seen only in infancy. There is usually a preceding bronchitis, but the clinical picture characteristic of involvement of the smallest bronchioles develops with great rapidity. The principal symptoms are high fever, pallor, cyanosis, and extremely rapid breathing.

The most characteristic symptom is the extreme dyspnea. The respiration is more rapid in this disease than in any other febrile affection, often reaching 100 or more per minute. It is very labored, with marked inspiratory retraction in the region of the epigastrium, and movement of the alae nasi. The pulse is rapid, but is not increased in rapidity nearly so much as is the respiration. Expiration is labored as well as inspiration.

At the beginning of the attack the infant seems strong enough, but prostration comes on rapidly, and the respiration becomes shallower, and the cough weak and infrequent. The children become

pale, with cold extremities, and usually show a notable cyanosis of the lips and finger tips. Vomiting and convulsions are often seen at the onset; later there is a marked apathy.

The physical signs in the lungs are quite characteristic. At the onset, even after the breathing has become very rapid and labored, the signs on auscultation are surprisingly slight. Only a few scattered high-pitched, sibilant râles are heard. Later these high-pitched sibilant râles are heard all over the chest, but *crepitant râles are noticeably absent*. The percussion is normal. The respiratory murmur and the tactile fremitus are notably diminished in intensity.

The condition seen in capillary bronchitis cannot last long. Probably in the majority of cases it represents only a stage in the development of a bronchopneumonia which is usually fatal. The development of bronchopneumonia cannot always be recognized clinically. It is usually characterized by the appearance of numerous *crepitant rales* throughout the chest, and by the rapid increase in the seriousness of the patient's general condition. In some cases, however, the complete clinical picture of capillary bronchitis as just described develops, persists from twelve to twenty-four hours, and then rapidly disappears, giving place to the picture of bronchitis of the medium-sized tubes. These cases usually recover. As autopsy reports have shown the possibility of an actual capillary bronchitis without bronchopneumonia, it is safe to assume that it can develop and not extend to a fatal pneumonia, but pass off as an ordinary bronchitis.

DIAGNOSIS.—Mild tracheo-bronchitis, and the common bronchitis of infancy, offer little difficulty in diagnosis. The presence of diffuse râles, without other physical signs, is diagnostic of bronchitis. Capillary bronchitis, in its earlier stages, may resemble lobar pneumonia, as both are characterized by high fever and rapid breathing, with signs in the chest insufficient to account for the dyspnea. Although in capillary bronchitis the respiration is usually more rapid, and especially, more labored, than in lobar pneumonia, the differential diagnosis cannot be made with certainty until the appearance of the diffuse fine sibilant râles characteristic of capillary bronchitis. Asthma is excluded, because in it the dyspnea is notably expiratory, and high fever is absent. Bronchopneumonia usually shows fine crepitant râles. The diagnosis of capillary bronchitis rests on the combination of extreme dyspnea, with high-pitched dry râles.

PROGNOSIS.—The prognosis of mild tracheo-bronchitis is uniformly good. There is, however, in certain children, a liability to recurrent or prolonged attacks.

In general, the prognosis of the common infantile form of bronchitis, involving the medium-sized bronchi, is also good. Acute bronchitis

in itself is never a fatal disease, although in babies greatly enfeebled from other causes, it may be an additional factor sufficient to turn the scale against them. The chief danger comes from the liability of the process to extend to bronchopneumonia. This occurs most often in young infants, and especially in those suffering from rachitis, or some other process attended by malnutrition. As children grow older, the liability toward bronchopneumonia is greatly lessened. Bronchopneumonia is less likely to occur in cases of primary acute bronchitis, and in cases in which bronchitis is due to the involvement of the bronchi in a common cold, than in cases complicating measles and pertussis, or some other similar acute infection.

The prognosis of capillary bronchitis is very grave. Most cases probably develop into a fatal bronchopneumonia. Nevertheless, as long as there are no diffuse crepitant râles to be heard in the chest, there is a chance of sudden improvement, followed by eventual recovery.

TREATMENT.—Children with acute bronchitis should be kept in bed as long as there is any fever. The room should be kept at a constant temperature of 68° to 70° F., and should be well ventilated, with some device, such as a window-board, allowing an open window with direct communication with the outside air. The windows need not be wide open, as there is no evidence of value from the cold air treatment of bronchitis, and the air from the window should not be allowed to blow directly upon the child. Children with slight fever and no constitutional symptoms, may be allowed to sit up in bed for part of the day. At such times they may wear a woollen dressing gown, but should never be allowed to sleep in one.

With older children, if there is little or no fever, the diet need not be reduced to any great extent. With a temperature over 100° F., or with any constitutional symptoms, there should be a light diet, with milk, toast, broths, cereal gruels, and fruit juices. In breast-fed infants the amount of food taken should be slightly reduced by shortening the nursing period, and the milk should be diluted by giving boiled water before each nursing. In bottle-fed infants, the strength of the food should be reduced to three-quarters or one-half that formerly taken.

Steam inhalations are the most effective therapeutic measures in acute bronchitis, particularly in its early stage. They are given in the child's crib, made into a tent by means of a sheet, the steam being introduced by means of a croup kettle, as described under the heading of Acute Laryngitis. Creosote, ten drops, or compound tincture of benzoin, one teaspoonful, may be added to a quart of water in the kettle. Severe cases should be steamed for fifteen or twenty minutes every two hours. Mild cases in older children need only be steamed at bedtime.

Counterirritation over the thorax is a useful therapeutic measure in all but the mildest cases. The best form of counterirritation is obtained by means of the mustard plaster, or rather, jacket, made as described in the section on therapeutics. The plaster should remain in contact with the skin for ten minutes, just long enough to produce a blush. It should be applied twice daily. As the skin becomes more sensitive, the proportion of mustard in the plaster must be reduced.

Drugs are less important than other measures in the treatment of acute bronchitis. None of them has any demonstrable influence in shortening the course of the disease. The only symptom requiring treatment is the cough. During the early stage, when the cough is dry and racking, ipecac is the best alleviating remedy, given frequently in small doses. If the cough is very severe and annoying, some opiate, such as paregoric or Dover's powder should be given in addition, in doses proportioned to the age of the child. I am in the habit of ordering the following prescription in the early stages of acute bronchitis.

R

	1ST YEAR	2ND YEAR	2-5 YEARS	5-12 YEARS
Wine of Ipecac.....	℥ ss	℥ i	℥ i ss	℥ ii
Paregoric.....	℥ ii ss	℥ v	℥ vii ss	℥ x
Sweet Spirits of Nitre.....	℥ ii ss	℥ v	℥ vii	℥ x
Water.....ad	℥ iv	℥ iv	℥ iv	℥ iv

M. Sig. Teaspoonful every three or four hours.

In the later stage of the disease, syrup of hydriodic acid in doses of 10 drops in the first year, 20 drops in the second, and half a teaspoonful to older children, is given three or four times a day instead of the ipecac; paregoric or Dover's powder may be given in addition, if the cough is severe.

In capillary bronchitis, more vigorous treatment must be employed. The most effective therapeutic measure is the mustard bath, or mustard pack, prepared as described in the section on Therapeutics. (Vol. I, Division II.) The baths or packs should be given for ten minutes at a time, and repeated if necessary. Between these treatments, ordinary hot packs may be used. It is usually necessary also in capillary bronchitis to give stimulants. The best stimulant in these cases is caffein-sodium-benzoate, given subcutaneously in doses proportioned to the age of the child. Intravenous injections can easily be given in infants with open fontanelles through the use of the longitudinal sinus. Camphor given intravenously is sometimes of value as a stimulant in very severe cases. Oxygen inhalations may be used if there is much cyanosis.

Children with acute bronchitis should be kept in bed as long as there is fever, and should be kept indoors as long as râles are heard in the lungs. During convalescence, one should gradually accustom

them to the breathing of cold air, by lowering the temperature of their sleeping rooms at night, taking care that they do not become uncovered. When râles have disappeared, they should begin to go outdoors daily, even though some cough persists.

The treatment between the attacks of bronchitis aimed at reducing the predisposition to frequent attacks, is the same as that used in the prevention of colds, and is described under acute rhinitis.

FIBRINOUS BRONCHITIS

During the course of what may appear to be an ordinary bronchitis, in rare instances a fibrinous form of bronchitis has been met with. In this variety masses of fibrin in the bronchi form casts of various extent according to the number of the bronchi which are affected. Similar fibrinous casts of the bronchi may be found in cases of diphtheria of the larynx by direct extension to the bronchi, but do not represent fibrinous bronchitis.

The disease may run a short course of days or weeks, but is usually chronic and may last for years. The paroxysms may also be periodic.

The diagnosis can be made only when portions of the casts have been expectorated.

TREATMENT.—The treatment is chiefly by the inhalation of steam or of atomized lime-water, and by supporting the strength with proper nourishment and stimulants until the disease has run its course.

CHRONIC BRONCHITIS

ETIOLOGY.—Chronic bronchitis may result from a series of attacks of acute bronchitis, or from a number of other causes. Among these may be mentioned various affections of the lungs, diseases associated with malnutrition such as rachitis, and prolonged attacks of pertussis.

PATHOLOGICAL ANATOMY.—The pathological conditions occurring in chronic bronchitis vary greatly in degree, and the lesions found at the post-mortem examination are often slight in comparison with the severity of the symptoms during life. In most cases there is a considerable production of mucus, pus and serum. In cases which have lasted for a long time, in addition to the inflammatory process affecting the walls of the bronchi there may be a dilatation of one or more bronchi, and the muscular coat may be thickened or thinned. Emphysema may also result.

SYMPTOMS.—The symptoms of chronic bronchitis are very much the same as those of acute bronchitis, except that the temperature is not so apt to be heightened, while the general symptoms of malaise, anorexia, and loss of weight are more prominent. In

severe and prolonged cases in which emphysema is present, the thorax may assume the position of full inspiration, the ribs being permanently raised and the antero-posterior diameter of the chest increased. The physical signs are the same as in acute bronchitis, so far as the râles are concerned. The resonance is usually normal except when the chronic process has produced emphysema, in which case there are areas of hyperresonance often associated with a tympanic tone. Occasionally atelectasis of considerable areas of the lungs may take place, with a resulting diminution of the respiratory sound. This occurrence may in some cases prove to be serious, but in others the accompanying symptoms are mild, and the alveoli may again return to their normal degree of inflation.

There is one form of bronchitis which, from its duration, may be called chronic, and yet which, from the very slight degree of constitutional symptoms that accompany it, corresponds rather to a sub-acute affection. In these cases, which usually occur in infancy and in early childhood, the child often appears quite well, but for long periods of weeks, or whenever it is exposed to a damp atmosphere, a loud wheezing will be heard in the chest. Auscultation will reveal the presence of sonorous râles everywhere, and in this variety, as well as in other forms of chronic bronchitis, a roughened sensation may sometimes be felt on palpation during respiration.

DIAGNOSIS.—The differential diagnosis is to be made from chronic affections of the lungs in which the thickening of the interstitial tissue has taken place with a resulting diminution of resonance and from the condition in which the bronchi are dilated. In the latter case there are accompanying symptoms of a profuse exudation of purulent matter.

Chronic bronchitis is also to be distinguished from reflex coughs of a nervous character, unaccompanied by any disease of the respiratory tract. Causes for such reflex coughs may be found in irritation of the pharynx and ear, from chronic gastric indigestion, from pulmonary congestion, from the disturbances in circulation due to cardiac disease, and, finally, from pressure upon the bronchi of enlarged mediastinal lymphnodes.

PROGNOSIS.—The prognosis of chronic bronchitis varies according to the cause. When it is secondary to disease of some other organ, it depends entirely upon the prognosis of that disease. In rachitic children the prognosis is unfavorable, and in them a bronchopneumonia is especially liable to develop, with a fatal issue. In cases which are the result of acute bronchitis in individuals otherwise healthy, the prognosis is favorable, provided the proper treatment can be carried out. As emphysema in chronic bronchitis is

rare in children in comparison with adults, the chances for recovery in the former are correspondingly good.

TREATMENT.—The treatment of chronic bronchitis is essentially climatic. The children should be kept in a warm dry climate for some months after the bronchitis has entirely disappeared. Especial care should be taken that the child is suitably protected by flannel undergarments. When other treatment is required, as a rule, tonics will prove of more benefit than the drugs which are usually administered for their direct effect upon the bronchial mucous membrane.

BRONCHOPNEUMONIA

(Lobular Pneumonia; Catarrhal Pneumonia.)

Bronchopneumonia is particularly a disease of infancy, and ranks with gastrointestinal disease and tuberculosis as one of the three diseases chiefly responsible for the high mortality of the first two years of life. The disease may occur in older children, but is very much less common, and much less fatal.

GENERAL PATHOLOGY.—From the point of view of etiology, bronchopneumonia is not a distinct disease, but takes its name from the character of the lesion found in the lung. This lesion involves the finer bronchi and the alveoli surrounding them, and is thus sharply distinguished from the lesion of lobar pneumonia, in which the inflammatory process originates in the pulmonary alveoli, and spreads rapidly through the lung tissue, without involvement of the bronchi. It appears then that the infecting micro-organisms in bronchopneumonia reach the alveoli of the lung through the medium of a bronchitis, which may originate in the bronchioles, or extend to them from the larger bronchi above. The disease is called "catarrhal pneumonia" from the character of the exudate, which is much like that seen in infections of the mucous membrane of the bronchi and upper air passages, and differs markedly from the fibrinous exudate seen in lobar pneumonia. The disease is also called "lobular pneumonia," from the distribution of the alveolar exudate, which fills the various pulmonary lobules surrounding the terminal bronchi, and is not distributed to a single lobe, as in lobar pneumonia. The amount and distribution of alveolar infiltration, and the histological character of the exudate, differ somewhat according to the nature of the infection.

There is every evidence that in bronchopneumonia the inflammatory process originates in the bronchi, and that the alveoli are involved by extension. The majority of cases of bronchopneumonia are obviously secondary to some form of bronchitis, the bronchitis itself being often secondary to some general infection. Certain cases of bronchopneumonia are called primary, but only on clinical grounds,

because the development of clinical evidences of bronchopneumonia is the first manifestation noted, with no preceding symptoms of bronchitis. From a pathological view-point these cases are not primary, but are to be explained on the ground that the terminal bronchioles are first involved, and that extension to the surrounding alveoli takes place so rapidly that their involvement is practically simultaneous with that of the bronchioles.

BACTERIOLOGY.—A great variety of microorganisms have been found associated with the lesions of bronchopneumonia. Among the most common are the *streptococcus*, the *pneumococcus*, the *staphylococcus aureus*, the *bacillus influenzae*, and the *tubercle bacillus*. Among the rarer ones are the *bacillus mucosus capsulatus* (Friedlander's bacillus), the *typhoid bacillus*, and the *bacillus of diphtheria*. Our means of judging the etiological rôle of these various microorganisms are very imperfect. Sputum cultures, and cultures taken post-mortem from the lungs are very likely to show the presence of more than one variety of bacteria, as is commonly the case in any lesion having free communication with the outside world. In such cases, it is difficult to tell whether the chief rôle in exciting the inflammation was played by one or by more than one variety, and which varieties represent secondary invasion of the lesions without etiological significance. Sometimes the predominance of a single variety suggests that it represents the etiological factor. Some varieties produce lesions peculiar to infection with that particular microorganism. These cases may be set apart as distinct diseases, with a definite specific etiology. In the majority of cases, however, we cannot know which if any microorganisms played the primary infective rôle, and must assume that the process represents a mixed infection.

CLASSIFICATION.—I believe that to a certain extent, a classification of the bronchopneumonias can be made upon an etiological basis, and that such a classification affords a useful basis for clinical description, and for considerations of prognosis and treatment. The basis for this classification is a series of bacteriological investigations which I have been carrying on at the Infants' Hospital in the last twelve years.*

Two varieties of bacteria have lesions peculiar to infection with that particular organism. These are the tubercle bacillus, and Friedlander's bacillus. These two forms may at once be differentiated as distinct etiological varieties of bronchopneumonia. There are three varieties in which a particular organism is the predominating, if not the exclusive organism found in post-mortem cultures. It is true that all of these same organisms are also found associated with

* The preliminary report of this investigation was published in the Boston Medical and Surgical Journal, May, 7, 1908, p. 631. The further results have not been published, but are confirmatory.

other varieties, and not predominating. It is also true that the lesions found in such cases are not characteristic. Nevertheless the clinical type in those cases in which the organisms greatly predominated has shown distinctive features with such frequency, that I believe they can be conveniently classified as distinctive forms of bronchopneumonia. The three organisms which thus appear to enact the chief rôle and to produce a definite clinical picture in certain cases, are the pneumococcus, the streptococcus, and the bacillus of influenza.

There remains a class of cases which still constitutes a majority of the bronchopneumonias of infancy, which we can only designate as mixed infections.

If it were possible in a textbook to adhere rigidly to an etiological classification of disease, the types of bronchopneumonia thus differentiated upon a basis of specific etiology should be considered, each under the proper etiological heading. They should be considered under tuberculosis, pneumococcus infection, streptococcus infection, influenza, and so forth. Such an arrangement in a textbook, however, has grave disadvantages. The various forms of pneumonia have been classified for generations on an anatomical basis. The terms lobar and bronchopneumonia have been continued by long usage. In diseases in which the clinical description depends more upon the character of the lesion and the organ involved, than upon the type of the infecting organism, description under etiological headings is difficult. It is better to describe the various forms of bronchopneumonia together, so that their clinical resemblances and differences can be brought out sharply. It is for this reason that both bronchopneumonia and lobar pneumonia are here described under diseases of the lungs. For the same reason tuberculous bronchopneumonia, of which the clinical manifestations are essentially those of bronchopneumonia rather than of tuberculosis, is described here, in comparison and contrast with other etiological varieties of similar pulmonary lesions.

The bronchopneumonias will be considered under the following classification:

ETIOLOGICAL CLASSIFICATION OF THE BRONCHOPNEUMONIAS

- | | |
|---|------------------------|
| 1. Common Secondary Bronchopneumonia..... | Mixed Infection |
| 2. Tuberculous Bronchopneumonia..... | Tubercle Bacillus |
| 3. Influenza Bronchopneumonia..... | Bacillus Influenzae |
| 4. Acute Primary Bronchopneumonia..... | Pneumococcus |
| 5. Terminal Bronchopneumonia..... | Streptococcus |
| 6. Friedlander's Pneumonia..... | Bacillus M. Capsulatus |

SECONDARY BRONCHOPNEUMONIA

This is the common type of bronchopneumonia. It is seen most frequently in infants, but occurs in older children.

ETIOLOGY.—In this type, bacteriological study shows a mixed infection. Pneumococci, staphylococci, streptococci and influenza bacilli are the organisms most frequently found in various combinations. Etiologically it has the same relation to infection of the lungs as have rhinitis, pharyngitis, laryngitis, and bronchitis to infection of the higher air passages. It is always secondary to bronchitis, and represents an extension of the process from the medium-sized bronchi to the bronchioles and their surrounding alveoli. Sometimes this extension occurs so rapidly as to give the impression of a primary process in the alveoli, but this is probably never the case in this type. The disease is always secondary. It may represent the extension of a primary infection of the upper respiratory passages, or of a primary bronchitis, to the lung tissue. It may be secondary to recognized infectious diseases which involve the air passages. In the order of frequency, it complicates measles, pertussis, and diphtheria. It may more rarely complicate recognized infections not primarily involving the upper air passages, such as infectious diarrhea, scarlet fever, erysipelas, and typhoid fever. It may be caused by inhalation of foreign substances. The predisposing causes of this type of bronchopneumonia are described in detail under Bronchitis. The disease is most common in the first year. After the second year its frequency diminishes rapidly.

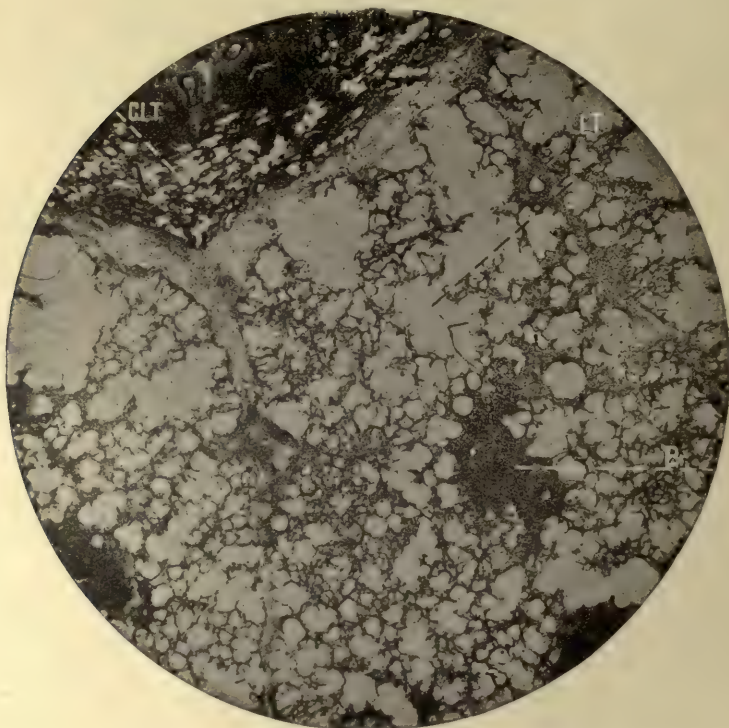
PATHOLOGICAL ANATOMY.—The essential lesion is exudate into the terminal bronchioles and their surrounding alveoli. Congestion precedes the exudation. The exudate consists of polynuclear leukocytes, mucus or serum, and in smaller numbers, lymphocytes, endothelial leukocytes, desquamated epithelial cells, and red blood corpuscles. Thus small areas of consolidation are formed through the lung tissue. In infants there are almost always scattered through the lung areas in which the alveoli not involved in the consolidation are emphysematous. There may be occasionally also areas of atelectasis, due to occlusion of the bronchial lumen through swelling of the mucous membrane.

The areas involved go through the various stages of congestion, consolidation, and resolution, although the process may terminate at any stage. The involvement of the lung tissue is very variable in amount. There may be only isolated nodules of consolidation surrounding the bronchioles, or there may be confluence of the consolidated areas, so that larger areas of consolidation are formed.

The process is usually bilateral, and diffuse. Some parts of the lungs are likely to be more affected than others, particularly the lower lobes posteriorly, or the posterior parts of both upper and lower lobes. Emphysema is found more in the anterior portions of the lobes. It is usually vesicular in character.

Death, or resolution may occur at any stage. Resolution may take place in one or two weeks, or it may be delayed for five weeks or more, and still be complete. It may, after delay, be only partial, with relapses or recurrent attacks. In such cases, there may finally develop a chronic interstitial pneumonia, or the unresolved areas may become the seat of secondary tuberculous infection.

FIG. 183



Broncho-pneumonia complicating measles. Early stage. C. L. T., consolidated lung-tissue; Br., bronchiole; L. T., emphysematous lung-tissue

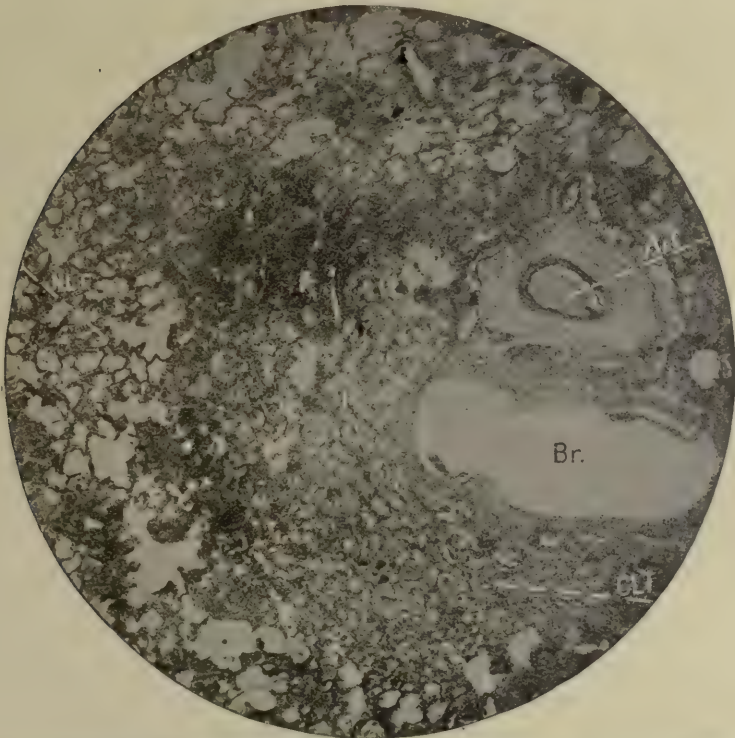
Pleurisy, of a varying degree of severity, is usually found over large confluent areas of consolidation. The bronchial lymphnodes are enlarged and congested. Gangrene of the lung is rare, but abscesses of the lung are not uncommon.

SYMPTOMS.—The symptoms of bronchopneumonia vary greatly in their onset and course. In many instances the bronchopneumonia is secondary to some other disease so that the symptoms are necessarily modified by those of the initial affection. Thus, when the bronchopneumonia arises in the course of diphtheria, the symptoms are often obscured by the severity of the general symptoms of the diphtheria. When bronchopneumonia is secondary to measles or

to pertussis, although at times its onset is difficult to detect, yet, as a rule, the rapid respiration, the marked and continuous rise of temperature, and the evident exacerbation in the severity of the pulmonary symptoms, usually permit a diagnosis to be made even before the physical signs have become prominent. Its onset, however, in measles is, as a rule, rapid, while in pertussis it is slower and more insidious.

The group of symptoms which characterizes a bronchopneumonia arising during the course of bronchitis is somewhat more definite. In place of the moderate temperature and the absence of signs of

FIG. 184



Broncho-pneumonia secondary to diphtheria. Br., bronchus; C. L. T., consolidated lung-tissue; N. L. T., lung-tissue nearly normal; Art., artery

serious disease which are usually met with in the course of an ordinary bronchitis, when bronchopneumonia supervenes the temperature rises, the pulse and respirations are increased in frequency, the alae nasi dilate, there is more or less cyanosis, the cough becomes more frequent and painful, and the general aspect of the patient is that of one suffering from an affection of a severe type.

ONSET.—The onset is rarely sudden, and there is no chill as a

rule. The child appears fretful and restless. The temperature rises and is very variable. There is cough, dyspnea, and rapid respiration. The physical signs are limited to scattered localized areas of fine and medium moist râles, and sometimes sonorous and sibilant râles.

TEMPERATURE.—The temperature in bronchopneumonia varies greatly, according to the extent and severity of the lesions. Corresponding to the intensity of the pneumonic onset, or to the especial disease which it complicates, the temperature rises rapidly or slowly and insidiously. The most common course in mild cases with gradual onset and terminating in recovery is for the temperature to rise gradually to 103° or 104° F., then to have a morning remission of three or four degrees for a number of days, and finally to fall irregularly by lysis. Although the remissions in the temperature during the active stage of the disease are often quite marked, yet, as a rule, the temperature does not at this time fall to normal. In the more severe and unfavorable cases the temperature becomes more and more elevated, even reaching as high as 107° F. Occasionally the temperature is reversed, the highest point being reached in the morning. When the temperature instead of remitting remains high and steadily rises, the disease, as a rule, soon terminates fatally. Instead of the continued high temperature which occurs so often in fatal cases, a low temperature of only a few degrees above normal is sometimes met with, usually when the vitality is low and the power of reaction slight. The duration of the heightened temperature is very variable, and may last for a number of days or for weeks without the necessary result of the grave lesions of a more chronic process.

PULSE AND RESPIRATION.—The pulse and respiration, although increased in frequency, vary according to the severity of the disease and also according to the degree of nervous excitement. This latter is a very important element to be considered in determining the gravity of their rate. The pulse is at times very rapid, 160 to 180, and even higher; it usually varies from 130 to 150 or 160; although regular and full at first, it becomes weak and sometimes irregular as the disease progresses, and is very apt to remain rapid even after the temperature has declined and convalescence has been established. The respirations may be quickened by an unusually high temperature, but depend mostly upon the extent of the involvement of the alveoli. They vary from 50 to 80, but they may be even higher, and are accompanied by dilation of the alae nasi.

The respiration often shows a pause after inspiration instead of after expiration, as occurs in normal respiration, and is often accompanied by an expiratory moan. Temporary exacerbations and

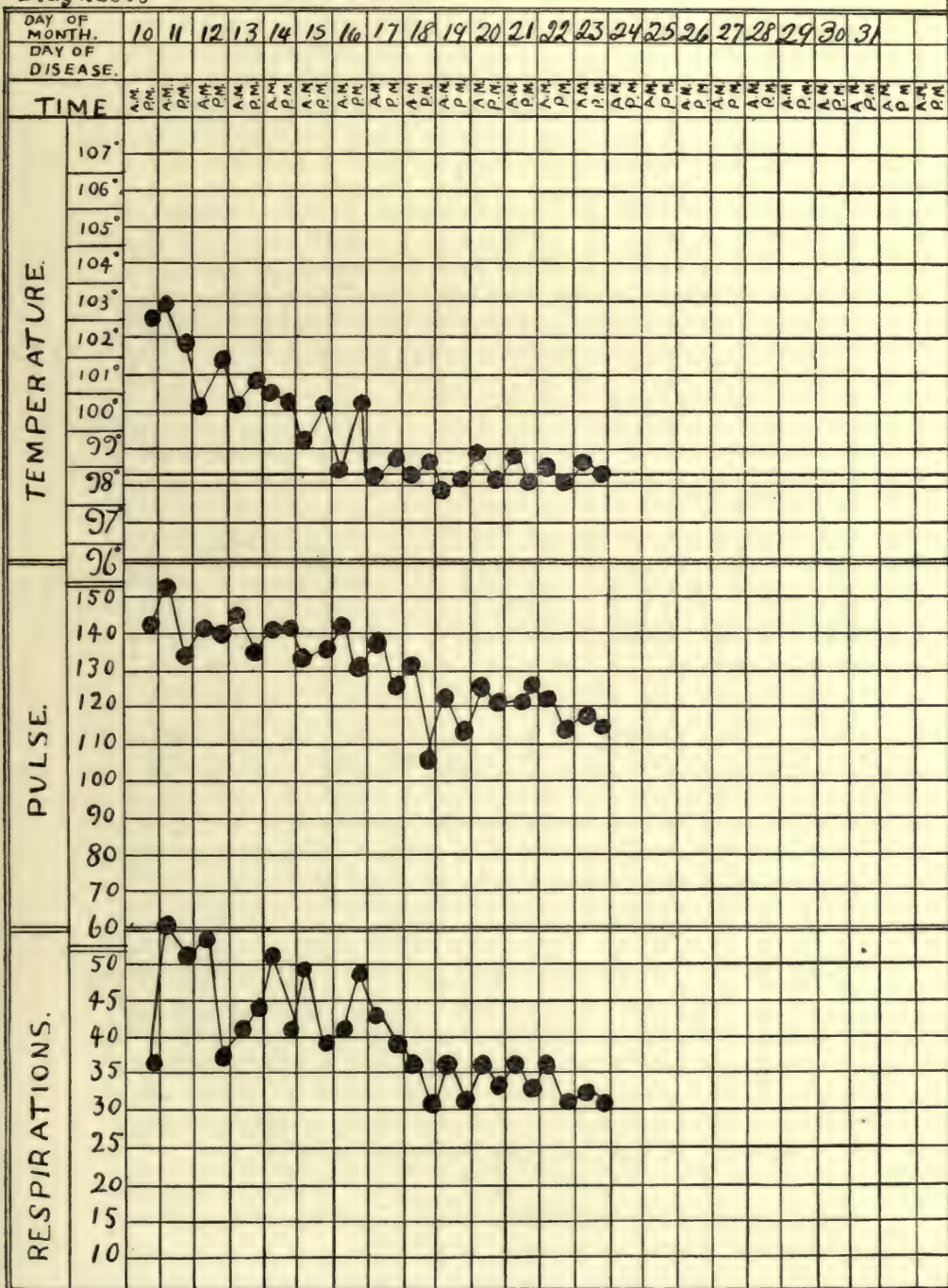


FIG. 185—Secondary bronchopneumonia
Diffuse crackling rales without definite signs of consolidation

Mr. Charles J. Tris coll

January

Diagnosis



changes in the rhythm of respiration are quite common in bronchopneumonia, and in some cases a Cheyne-Stokes type has been noticed. This sign is usually one of grave import. Recession of the epigastrium and of the intercostal spaces commonly occurs in bronchopneumonia, and varies according to the severity of the pulmonary lesions. In infants painful respiration is shown by a frown rather than by crying, while in young children it is shown by their whimpering and suppressed cries.

COUGH.—A frequent, short, hacking, and painful cough is a constant symptom from the beginning of the disease, and even after resolution has taken place this may continue for a long period. Infants and young children, even up to the age of seven or eight years, have often not learned to expectorate, so that we cannot, as in adults, judge of the character of the sputum.

GASTRO-ENTERIC SYMPTOMS.—Vomiting is at times met with, but rarely at the onset, and diarrhea is not uncommon. In certain cases disturbance of the gastro-enteric tract is present from the very beginning, and the intestinal disease is apparently as prominent a feature of the attack as the pulmonary symptoms. As the attack progresses the child loses much weight, the face often looks pinched, and at times during the height of the disease there is a certain amount of delirium, which in combination with other grave symptoms, such as uncontrollable diarrhea and a depressed temperature, is a serious symptom.

CYANOSIS AND DYSPNEA.—A symptom which occurs quite commonly in bronchopneumonia is cyanosis. This may not only arise from the interference with the oxygenation of the blood from the lesions involving the air-vesicles, but may also be produced by a temporary atelectasis of certain portions of the lungs. The cyanosis is often accompanied by attacks of dyspnea. When these symptoms result from atelectasis, the temperature, as a rule, does not rise, but may even be somewhat reduced, and areas of dulness may be detected on percussion. During these paroxysms the skin is often cold and moist. When the cause of the atelectasis, whether it be obstruction by plugs of mucus or pus or temporary exhaustion of the contractile powers of certain portions of the lungs, has been removed, the cyanosis and dyspnea pass away and the general symptoms improve. These symptoms may develop at various periods during the course of bronchopneumonia, and unless the atelectasis passes off within a few days a fatal issue is very apt to result.

BLOOD.—A leucocytosis is generally present if the bronchopneumonia is due to the pneumococcus or to mixed infections, and may be as high as 40,000, 50,000 or even 60,000.

PHYSICAL SIGNS IN THE CHEST.—In the early stages of secondary



FIG. 186—Secondary bronchopneumonia
Scattered crepitant râles, and two areas with slight dulness and bronchovesicular breathing

bronchopneumonia, and in the majority of cases throughout the disease, the physical signs usually associated with pulmonary consolidation are absent. On auscultation moist râles of all grades are heard over the chest. These râles may be diffusely scattered and heard over all parts of the chest, or there may be collections of râles in circumscribed areas. The râles are however, almost always bilateral, and show no tendency to be confined to any one particular lobe. They are usually most numerous over the lower lobes behind. The râles have a peculiar, crackling sound, seeming to come from a point intermediate between the ear and the chest. Fine crepitant râles are usually to be heard, but may be masked by the coarser crackles.

In a certain number of cases, in the course of the disease, definite signs of pulmonary consolidation develop in different parts of the chest. Sometimes definite dulness cannot be detected, but there are more or less extensive areas over which the respiratory murmur has a slight broncho-vesicular sound, or even a distinctly bronchial sound, in contrast to other portions. In other cases, small areas of dulness and bronchial breathing may be found. In still other cases, comparatively rare, there may be larger areas of dulness and bronchial breathing, and occasionally a very extensive area, even amounting to an entire lobe, may show these signs. These wide variations in the signs of consolidation are due to the amount of confluence of the solidified lobules. Autopsy findings suggest that a considerable degree of confluence is required to produce signs of consolidation in bronchopneumonia. This accounts for the fact that in the majority of cases, definite signs of consolidation are not found.

The areas of consolidation are most apt to be found over the lower lobes behind, and between the scapulae. There may be sharply defined areas in other parts of the lungs. The essential feature in the distribution of the signs, is that they show no especial tendency to be confined to a single lobe. Sometimes the only area showing signs of consolidation is in one lobe, but always the crackling râles, similar to those heard over the consolidated area, are heard in other parts of the chest.

TERMINATIONS AND COMPLICATIONS. RESOLUTION.—If the course of the disease is favorable, the pathological process in the areas of consolidation terminates in resolution, which is often more rapid in the individual areas than in lobar pneumonia, but may be delayed for several days or weeks as in the latter affection. In cases which recover, resolution takes place slowly and the lung gradually returns to the normal condition. Great weakness and prostration often last for a long time. Relapses are quite common.

SUPPURATION.—Resolution by suppuration is rare in the more

common forms of primary and secondary bronchopneumonias, and is limited almost entirely to cases of inhalation or deglutition bronchopneumonias, in which it is very frequent. Under the same conditions gangrene of the lung may develop.

CHRONIC FIBROID CHANGES.—These will be described separately under chronic bronchopneumonia.

TUBERCULOSIS.—Cases of bronchopneumonia with delayed resolution show a special susceptibility to infection by the tubercle bacillus.

OTITIS MEDIA.—This is a common complication in bronchopneumonia.

FIG. 187



Acute broncho-pneumonia. Female, 4½ years old. The black circles indicate areas of consolidated lung-tissue; the black spots indicate râles

PLEURISY.—Fibrinous, serous, or purulent pleurisy is not a very rare complication of this type of bronchopneumonia.

DIAGNOSIS.—In the differential diagnosis of bronchopneumonia, the principal conditions to be considered are acute bronchitis, lobar pneumonia, and tuberculous bronchopneumonia.

Acute Bronchitis.—It is not always possible to say with accuracy whether in an infant the process is acute bronchitis or secondary bronchopneumonia. Both diseases have more or less diffuse râles as the principal physical sign. When definite signs of consolidation are present, simple acute bronchitis can be excluded, but in the majority of cases such signs are not present. In general the diagnosis of bronchopneumonia rests on the greater severity of the clinical manifestations. The respiration is more rapid, the temperature is higher for a longer period, and the general constitutional symptoms are much more severe. Marked dyspnea, cyanosis, or a weak and



FIG. 188—Secondary bronchopneumonia; roentgenogram



FIG. 189—Secondary bronchopneumonia; roentgenogram



FIG. 190.—Bronchopneumonia. The plate shows infiltration of the lung tissue

rapid pulse, all point toward bronchopneumonia. The râles in acute bronchitis are rarely of the fine crepitant variety, while in bronchopneumonia the râles are either crepitant, or have the peculiar crackling sound so often associated with consolidation. Severe cases of acute bronchitis and mild cases of bronchopneumonia are nevertheless clinically not far apart. When the physician is in doubt, bronchopneumonia is probably the correct diagnosis. More cases of bronchopneumonia, as shown by autopsy findings, are diagnosed as bronchitis, than vice versa. The Roentgen ray examination of the chest is sometimes of aid. It will often show the diffuse infiltration of the chest characteristic of bronchopneumonia, but does not show bronchitis.

Lobar Pneumonia.—In typical cases, there are numerous points of clinical difference between secondary bronchopneumonia and lobar pneumonia. When the physical signs of lobar pneumonia are fully developed, the larger area of consolidation, confined to one lobe, with marked dulness, bronchial breathing, bronchophony, and crepitant râles confined to the solidified lobe, make the diagnosis unmistakable. Unfortunately, in infants and young children, the physical signs of lobar pneumonia are very slow in developing, and are often not at all pronounced at any stage. This is indeed an important feature of the differential diagnosis, for in secondary bronchopneumonia some physical signs, namely râles, are usually present from the beginning. In any case with fever and rapid breathing, if the examination of the chest is wholly negative, lobar pneumonia is the only form likely to be present.

In lobar pneumonia, the disease is primary, and the onset sudden with symptoms suggesting some general acute infection, and not pointing particularly to the chest. In common bronchopneumonia the disease is secondary, and the onset usually gradual, but nevertheless from the beginning the symptoms point unmistakably toward the lungs as the seat of the disease, cough and rapid breathing being the most prominent symptoms. In lobar pneumonia, the physical signs in the chest are at first slight or absent, and when they do develop, are usually confined to one lobe of the lungs. In bronchopneumonia râles are present from the start, and are usually widely scattered in different parts of the chest. In lobar pneumonia definite signs of consolidation usually develop eventually in some lobe. In bronchopneumonia definite signs of consolidation often never develop, and when they do, are of irregular and indefinite distribution. In lobar pneumonia the typical temperature curve is high and sustained; in bronchopneumonia it is very irregular, and not characteristic. In lobar pneumonia, while the respiration is markedly accelerated, severe dyspnea and cyanosis are uncommon; in bronchopneumonia they are often early symptoms. In lobar

pneumonia the typical course is comparatively short, with termination by crisis. In bronchopneumonia the typical course is longer, with gradual lysis.

The chief difficulty lies in the fact that in both diseases, atypical cases are quite common. Various features of one disease may resemble those usually found in the other. Both forms of pneumonia may even be present in the same case. The physician must take everything into consideration in forming a judgment. The Roentgen ray examination of the chest is of great value in the diagnosis of doubtful cases. In lobar pneumonia one area of shadow only is seen, in one lobe. In bronchopneumonia, while there may be one large shadow, there is usually evidence of diffuse pulmonary infiltration in other parts of the plate.

Tuberculous Bronchopneumonia.—The differential diagnosis between secondary and tuberculous bronchopneumonia, will be considered under the latter heading.

PROGNOSIS.—Age is a very important factor in the prognosis of bronchopneumonia. A large majority of the fatal cases occur in the first two years of life, and often run as high as 60 or 70 per cent. This high death rate rapidly diminishes after the third year, but is always much greater than that of lobar pneumonia. Bronchopneumonia causes more deaths in children than are due directly to other fevers, and is the most serious complication of the contagious diseases. The prognosis varies according to the disease in the course of which bronchopneumonia develops. It is most grave when it occurs in pertussis, especially in infants, and the younger the child the more fatal the disease. Next to pertussis, the gravity of the prognosis is greatest in measles and diphtheria. When it occurs in such diseases as rachitis and tuberculosis, or when the individual has not been well cared for, the prognosis is also very unfavorable.

I have already referred to the temperature as a prognostic sign in bronchopneumonia. According to Holt's observations, the highest mortality occurs among the cases of shortest duration, and the disease is universally fatal when its duration is shorter than four days. After this early period of danger is passed the prognosis becomes more favorable, the lowest death-rate in Holt's cases being met with in cases terminating in from eight to fourteen days. When the disease lasts for more than two weeks the chances of recovery are lessened every day that the temperature remains raised. The cases in which there is a very high temperature, 106° F., are usually fatal. When the disease is protracted, death generally occurs from exhaustion.

PROPHYLAXIS.—The general prophylaxis of bronchopneumonia

is the same as that of acute bronchitis. Every case of bronchitis should have careful attention. Bronchopneumonia is much more apt to develop in children when bronchitis is neglected.

TREATMENT.—This type of bronchopneumonia being a mixed infection, there is obviously no specific therapy available, and no immediate prospect of progress in this direction. Therapeutic endeavor must be directed at strengthening the general powers of resistance against infection, at assisting physiological functions injured by the disease, and at relieving particular symptoms.

GENERAL HYGIENE.—The general measures of hygiene and nursing which are desirable in every severe acute infection, are to be carried out in bronchopneumonia. While older children must be kept in bed, care must be taken that they have a frequent change of position; it is not advisable for them to lie on the back for several hours at a time. Infants should not be kept in their cribs so much in bronchopneumonia as in other acute fevers; for much of the time they may be held in the nurse's arms, and their position should be changed frequently. When the cold air treatment is not used, plenty of fresh air is essential in the treatment of all forms of pneumonia.

The diet should be managed as in all acute illnesses, with due regard to the liability to digestive disturbance. The aim should be to meet the caloric needs of the child while imposing the least burden on the digestive powers. It is sometimes difficult to get infants to take enough food. When breast-fed infants will not take the breast properly, the milk must be obtained by pumping. The giving of food must often be assisted by the use of the spoon, medicine dropper, or a Breck feeder, and in some severe cases in infants, tube feeding has to be employed.

Alcohol is useful in bronchopneumonia. Although modern research denies to alcohol any value as a circulatory stimulant, clinical experience continues to suggest that it has a distinct benefit, particularly in the longer acute illnesses. Its chief value is probably as an easily utilizable food, serving as a source of energy, and preventing tissue waste. I do not think its use should be a routine measure in every case, but it should be used in all cases in which the amount of food taken tends to fall below what is desired. Rye whiskey is a good form of giving alcohol to children, and may be given in doses of 20 to 30 drops every four hours to a child over one year old.

Counterirritation is one of the general measures widely advocated in bronchopneumonia. The irritation of the skin is sometimes evidently annoying to the child, and I do not believe its therapeutic advantages are great enough to call for the use of counterirritation as a routine measure. I use it only in those cases in which the pneumonia is accompanied by signs of extensive bronchitis of the

larger tubes. It is best given in the form of the mustard paste jacket described in the section on therapeutics. Simple rubbing of the chest with camphorated oil is often equally effective.

The bowels should be watched carefully in bronchopneumonia. Abdominal distention increases the difficulties of the patient. One bowel movement daily should be insured.

COLD AIR TREATMENT.—The principal demonstration of the value of cold air, has been made in lobar pneumonia. It has been definitely shown that the therapeutic benefit comes from the actual breathing of cold air, and that it consists in raising the blood pressure, which tends to fall in pneumonia through toxic vasomotor paralysis. There is no doubt that the cold air treatment has a similar value in bronchopneumonia. The only questions are whether cold air may not have an injurious effect on the attendant bronchitis, and whether or not it may depress the vitality of very young or feeble infants. As to the first question, I believe there is some doubt, and I do not use the cold air treatment in cases having extensive bronchitis of the larger bronchi, unless the condition of the patient suggests serious depression of the circulation from the toxemia of the disease, as shown by weak and rapid pulse. As to the second question, in my experience infants, even when young and delicate, show no depression of the vitality from the breathing of cold air, when properly protected. I use it in all very sick cases. Any signs of laryngitis are, however, an absolute contraindication to its use. The method of utilizing the cold air treatment is described under lobar pneumonia.

COUGH.—The best therapeutic measure for the control of the cough in bronchopneumonia, is steam inhalations. They cannot well be combined with the cold air treatment, and are most useful in the cases having marked attendant bronchitis, in which cold air is not employed. In very sick patients, the cold air treatment is more important than the treatment of cough, and I do not believe the cough should be treated unless it is frequent or severe enough to be an evident drain on the infant's vitality. It rarely should require any drug treatment. Expectorants should be avoided in bronchopneumonia. Opium or its derivatives are the only effective drugs against cough, and their disadvantageous action on the bowels, appetite, and digestion, make it best not to use them as a routine. An opiate should be given only if the cough is excessively frequent or severe.

FEVER AND NERVOUS IRRITABILITY.—The fever of secondary bronchopneumonia is of the remittent or intermittent type, and does not often require treatment. I do not believe that the antipyretic coal tar products, such as phenacetin or antipyrin should be used to combat fever in bronchopneumonia. They are depressing,

and may do more harm than good. Cold sponging, or cold packs are safer than the antipyretic drugs, but many children do not bear cold well, especially infants. These measures are only indicated in cases with hyperpyrexia, which in bronchopneumonia I should define as a temperature of 105° F. or over.

For nervous symptoms, such as restlessness and loss of sleep, the best treatment is tepid sponging at bed time. Opium is to be avoided, and I believe the coal tar products also are not advisable. The best drug in cases of nervous irritability is bromide of sodium, given in doses of four or five grains three times in twenty-four hours to a child of two years.

STIMULATION.—The most important symptoms requiring treatment in bronchopneumonia are those due to the effect of the toxemia on the circulatory system. Most cases are severe enough to require some stimulation, but it should not be given as a routine just because the child has bronchopneumonia. When the pulse is very rapid, but regular, and not of extremely low tension, the best stimulants are digitalis or strophanthus. The fluid extract of digitalis, more reliable than the tincture, may be given in doses of $\text{m} \frac{1}{2}$ every four hours, or the tincture of strophanthus in doses of $\text{m} \text{ i}$ every four hours, to a child one year of age. In bronchopneumonia the pulse often becomes not very rapid, irregular in force or rhythm, and easily compressible. Blood pressure testing is more difficult in children than in adults, but if performed, the blood pressure in cases showing this kind of pulse is found very low. The best stimulant is caffein. I usually use the caffein sodium benzoate, in doses of $\frac{1}{2}$ to i grain by mouth and of $\frac{1}{4}$ to $\frac{1}{2}$ grain hypodermically, to a child one year of age. Strychnin is widely recommended, but its therapeutic action is mainly as a respiratory stimulant. I do not use it in bronchopneumonia, unless there is a sudden respiratory failure.

When quick stimulating effect is desired, as sometimes happens when a patient is first seen, camphor may be given subcutaneously, $\text{m} \text{ ii}$ or iii of a ten per cent solution in oil.

For extreme dyspnea with cyanosis, oxygen may be given. It should always be combined with atmospheric air.

COLLAPSE.—Sudden attacks of general collapse are frequent in bronchopneumonia, with threatened circulatory failure. In such a case, I give the stimulation intravenously, into the longitudinal sinus, in all infants with open fontanelles. Caffein or camphor may be used. Adrenalin in doses of $\text{m} \text{ ii}$ or $\text{m} \text{ iii}$ of a i-1000 solution, given intravenously, is of great value for immediate action in sudden heart or respiratory failure. In addition to stimulant drugs, the hot mustard bath is often of value in collapse.

PROLONGED CASE.—When a case of bronchopneumonia runs a

long course with continued fever, the fresh air treatment should be carried out as for tuberculosis. If the fever subsides, but the pneumonia remains unresolved, with persistent general cachexia, a change of climate, in addition to the fresh air treatment, is indicated. In winter or spring the child should be removed to a warm climate; in summer, it should be taken to the mountains. Cod liver oil and iron are often valuable additions to the treatment in these prolonged, unresolved cases.

TUBERCULOUS BRONCHOPNEUMONIA

This is the commonest manifestation of the extension of tuberculous infection from the primary lesion seen in early life. Its pathology has been described in the section on Tuberculosis.

SYMPTOMS.—This form of bronchopneumonia may occur after a single attack, or after repeated attacks of what clinically appeared to be acute bronchitis, or secondary bronchopneumonia. It often develops as a sequel of one of the acute infections, particularly measles and pertussis. It may gradually develop as a sequel to a lobar pneumonia or bronchopneumonia which has remained unresolved. It may develop in a form apparently primary, although we know that it is really secondary to some latent primary lesion.

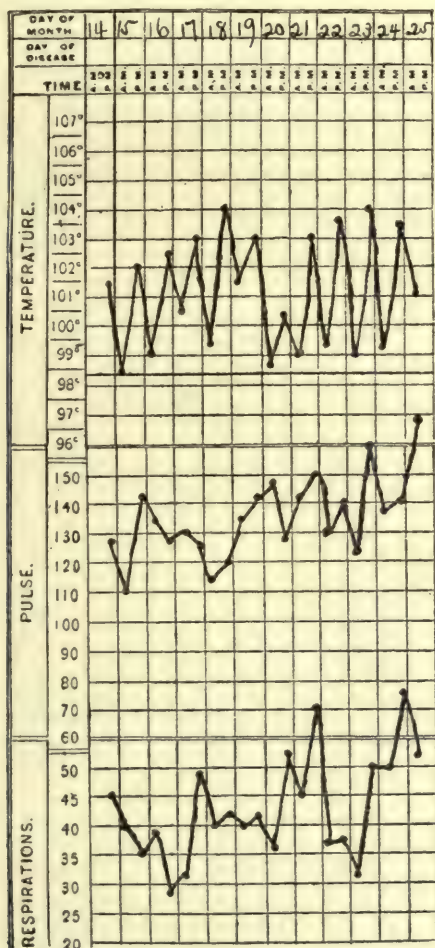
It is a disease which presents the greatest variability in the acuteness of its symptoms and course. The important symptoms are cough, rapid respiration, fever, progressive weakness and anemia. For convenience of clinical description it may be divided into three types, acute, subacute, and chronic.

ACUTE TYPE.—This type is usually indistinguishable clinically from secondary bronchopneumonia due to a mixed infection. It is seen almost exclusively in infants. The onset, symptoms, and course resemble the description of secondary bronchopneumonia given above. The physical signs in the lungs are the same, namely diffuse crackling and fine crepitant râles, and sometimes the formation of scattered areas of various extent, showing signs of consolidation. Two differences only, I have observed in many of these cases. First, the temperature curve is apt to show a more regular daily remission and exacerbation, of several degrees. Second, even when the patients are acutely ill, with very rapid respiration, there is not so much evidence of toxemia affecting the nervous system; the infants are brighter, and take more notice of their surroundings.

SUBACUTE TYPE.—This type is the commonest, both in infants and young children, and is the type which most commonly occurs as a sequel of measles and pertussis. In this form the onset is more gradual than in the common secondary bronchopneumonia, and the course is less rapid. Cough, moderate irregular fever, with scattered

moist râles in the lungs, may be present for a variable period, before the appearance of symptoms suggesting pneumonia. Eventually the respiration becomes rapid, and the fever ranges daily from about 100° to 102° F. Later it may go higher, and there may be temporary falls to the normal. The chart may still resemble that of the common

CHART 20



Tuberculous Bronchopneumonia, Acute Type

secondary bronchopneumonia, but sometimes it shows more wide and regular exacerbations and remissions, which are quite characteristic when present. Cough may become more severe, and sometimes paroxysmal. There is steady loss of weight and increasing anemia.

Although the respiration is accelerated in this type, the extreme labored breathing and cyanosis so often seen in simple broncho-

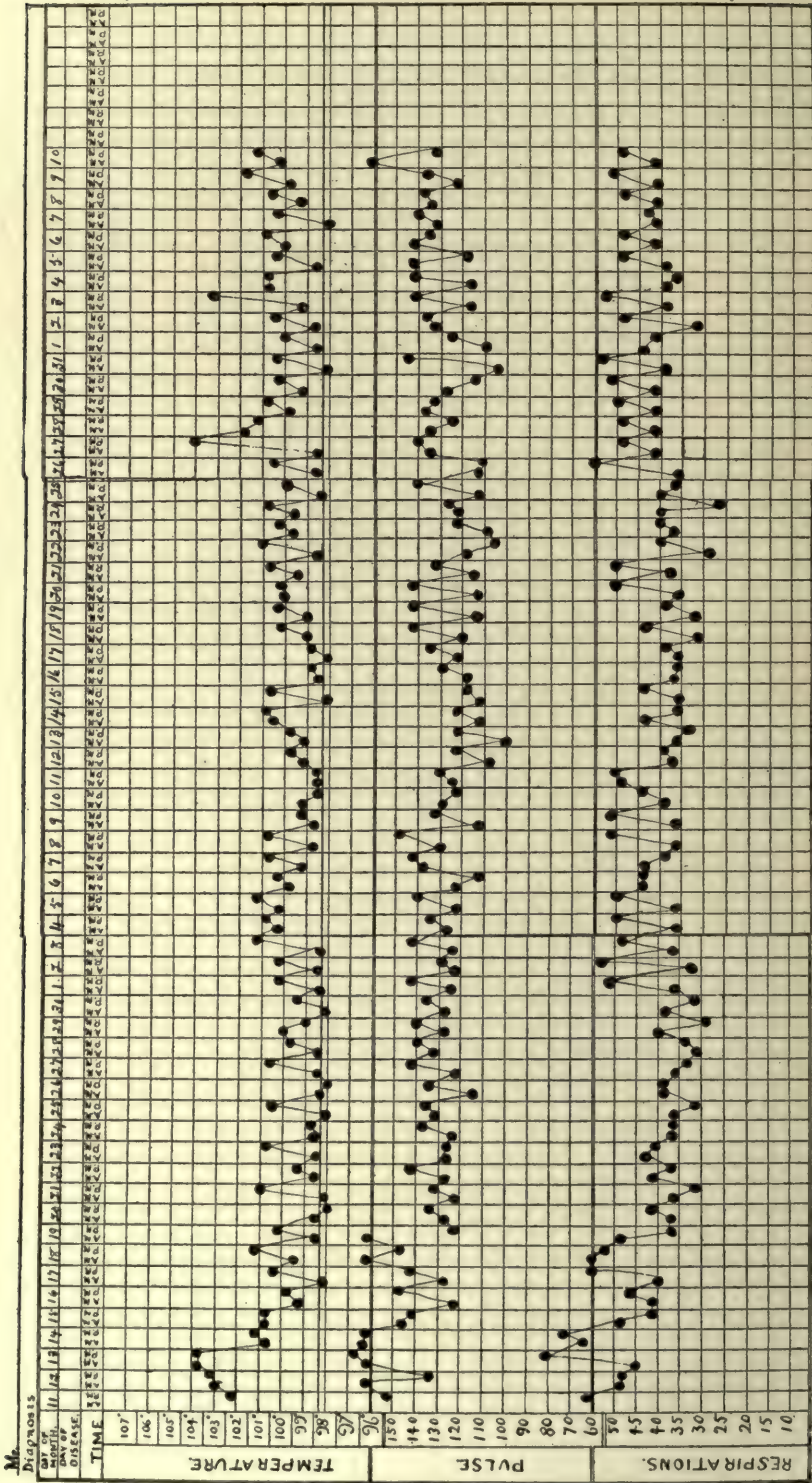


CHART 21—Tuberculous Bronchopneumonia, Subacute Type.



FIG. 191—Tuberculous bronchopneumonia, subacute type

pneumonia, are not seen until the end. In the early stages the pulse is rapid, but is not so seriously affected, and marked circulatory disturbance and collapse do not occur. The mental condition of the child is notably clear until near the end, unless tuberculous meningitis develops. I have seen children with tuberculous bronchopneumonia breathing 80 to the minute, still wanting to play with their toys.

The physical signs in the chest are not so widespread and diffuse as in the acute type. Some areas of the lungs usually appear to be free of râles. Definite areas showing dulness, bronchial breathing, and bronchophony, with crackling râles, always appear in this type. There may be one or more of these areas, in various parts of the chest. They remain for some time and tend to grow gradually larger in extent. The signs of consolidation may extend to form such large areas, that lobar pneumonia is suggested. The dulness on percussion is usually greater than in lobar pneumonia, and there is often flatness so marked as to suggest the presence of a pleural effusion. Cavity formation often occurs in the consolidated areas, as shown at autopsy. The signs of cavity are not often detected during life, as they are often small, or filled with thick creamy pus. Moist râles of all sizes are found at all stages, and pleuritic friction rubs are not uncommon.

The course of this type is prolonged. In the majority of cases, the progress is steadily downward until death occurs after a period usually varying from one to three months. As the fatal termination approaches, the temperature, pulse, and respiration gradually become higher, and emaciation becomes extreme. Death occurs from exhaustion, rather than from an active toxemia.

In some cases, after a more or less prolonged course, improvement occurs. In such cases, the anatomical changes consist in partial resolution, and in the development of the process in the lung called chronic interstitial or fibroid pneumonia. There is a slow convalescence, followed by apparent recovery. Most of the signs of consolidation gradually disappear, but often some cough, and some abnormal signs in the lungs persist for a very long time. These patients also do not regain their full health and vigor for a long period. They are liable to recurrent attacks of bronchopneumonia, which are apt to assume a more chronic type, with anemia and malnutrition in the intervals. Finally, complete recovery, except for possibly some abnormal signs in the lungs, may occur.

CHRONIC TYPE.—This type differs from the preceding mainly in the chronicity of its course. The clinical picture resembles the phthisis of late childhood and adult life, rather than bronchopneumonia. The usual diagnosis is chronic pulmonary tuberculosis, and this term is not a misnomer, unless restricted to the description of

the phthisis of adults. If so restricted, it should not be applied to the chronic form of secondary tuberculosis seen in young children, because the essential pathology of this condition differs markedly from that of phthisis. The pathological process is a bronchopneumonia, differing in no way from that of the more acute forms just described. It is only clinically that the disease resembles phthisis, on account of the prolonged chronic course sometimes seen in cases showing post-mortem the typical lesions of tuberculous bronchopneumonia.

In this type there is cough, fever, and progressive emaciation and anemia. The temperature is often moderate, and may be normal for days together, but from time to time, sudden rises of temperature occur. The respiration is not notably accelerated. The progressive cachexia resembles that seen in phthisis; there may even be night sweats.

The signs in the lungs are much like those seen in the subacute type, but are usually more localized. In the early months of the disease, there is often only one area of consolidation, which gradually grows larger, until a whole lobe or more may be involved, showing marked dulness or flatness, bronchial breathing, bronchophony, and crackling râles. Later, other areas may appear.

The course is prolonged, covering a period of months. Death may occur from gradual exhaustion, or from the intercurrent of a more acute attack. At any stage, the process may be arrested, recovery gradually occurring by partial resolution, and chronic fibroid healing.

DIAGNOSIS.—In differential diagnosis, tuberculous bronchopneumonia is to be distinguished from *common secondary bronchopneumonia* due to a mixed infection, from *lobar pneumonia*, from *empyema*, from *unresolved pneumonia*, and from *phthisis*.

In any case, if at any time previous to the development of the symptoms and signs suggesting tuberculous bronchopneumonia, a diagnosis of chronic tuberculosis of the lymphnodes has been made, the diagnosis of tuberculous bronchopneumonia is greatly strengthened. Even after the development of the symptoms and signs suggesting tuberculous bronchopneumonia, if there is evidence of enlargement of the bronchial lymphnode groups, tuberculous bronchopneumonia is the probable diagnosis. Evidence of primary tuberculous infection must be sought by a careful testing for d'Espine's sign, and by a roentgenogram of the chest. If the former is positive, or if the roentgenogram shows definite lymphnode enlargement, tuberculosis is probable. The von Pirquet test, if applied after the development of bronchopneumonia, is often negative, and throws no light on the diagnosis. It is most often positive in the chronic type, and if



FIG. 192.—Tuberculous bronchopneumonia; roentgenogram

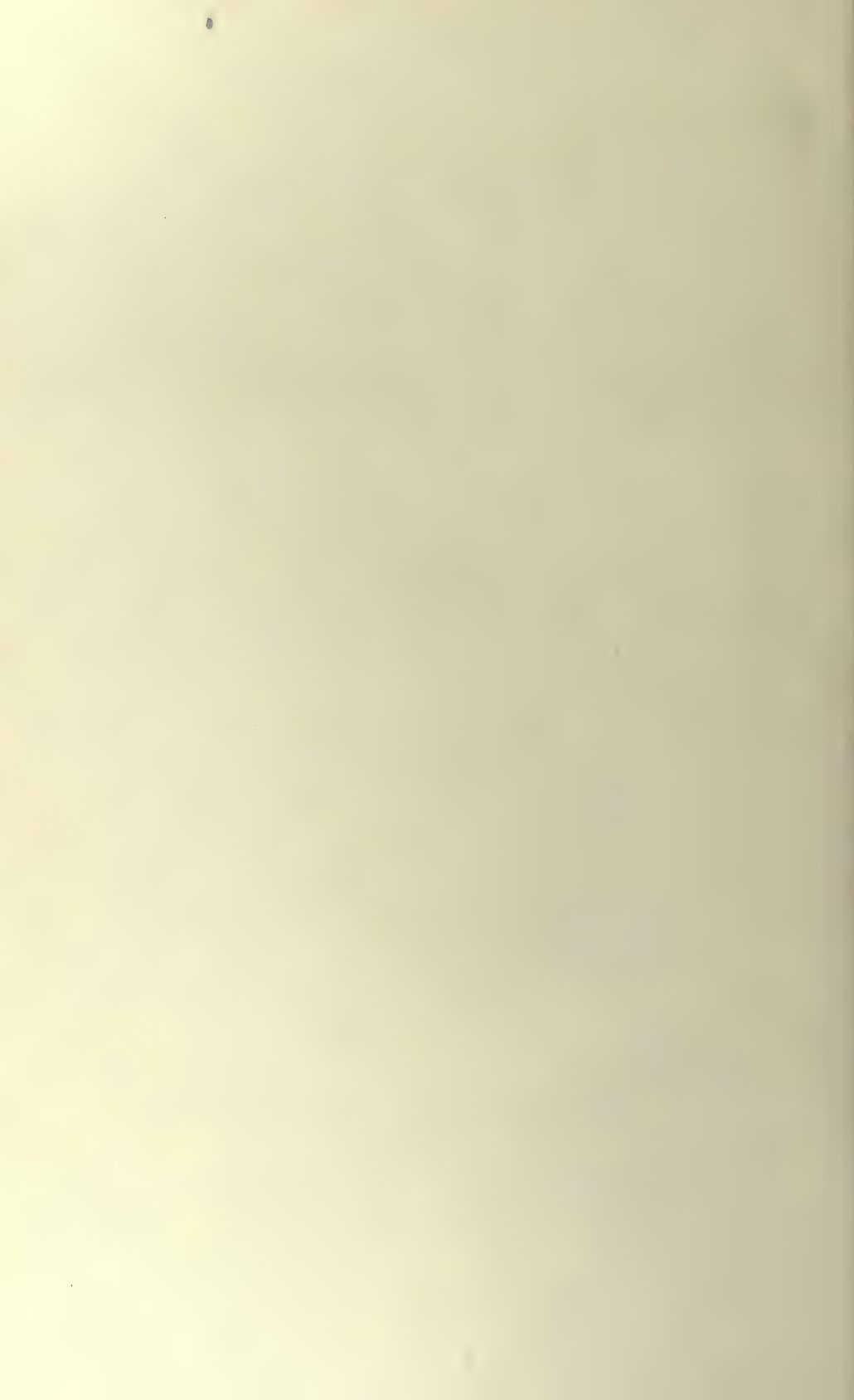




FIG. 193—Tuberculous bronchopneumonia; roentgenogram

this is the case, the diagnosis is much helped. Sputum examination is not often of much assistance in tuberculous bronchopneumonia. The difficulties of obtaining sputum in infants and young children may be overcome (see Div. II, Section on Diagnosis), but even then, in tuberculous bronchopneumonia the bacilli are not coughed up in the sputum with anything like the frequency that they are in phthisis. Probably they are only coughed up when cavities are present, and even then, the cavities often do not communicate with a bronchus. Of course, in those rare cases in which tubercle bacilli can be found in the sputum, they are diagnostic of a tuberculous process, and it is only necessary then to differentiate between bronchopneumonia and phthisis.

Common Secondary Bronchopneumonia.—The acute type of tuberculous bronchopneumonia cannot often be distinguished from bronchopneumonia due to a mixed infection. The former should be suspected if there is any evidence of lymphnode enlargement, or of previous chronic tuberculosis, if the temperature curve shows *regular* exacerbations and remissions, and if the apathy and other toxic manifestations are slight in comparison with the apparent severity of the respiratory involvement.

The subacute type is distinguished from simple bronchopneumonia by its more prolonged course, by the greater localization of its pulmonary signs, by its *tending to show large persistent areas of consolidation*, by the absence of severe circulatory disturbance and mental dulness, and sometimes, by the appearance of a "hectic" temperature curve with regular daily exacerbations and remissions.

The clinical picture of the chronic type does not suggest bronchopneumonia at all.

Lobar Pneumonia.—The subacute and chronic types of tuberculous bronchopneumonia frequently show large areas of dulness, bronchial breathing, bronchophony, and crackling râles, corresponding in extent to the consolidation of a lobar pneumonia. The diagnosis of tuberculous bronchopneumonia depends mainly on the more gradual onset, the more irregular temperature curve, the slower course, and on the more pronounced character of the dulness, which often amounts to flatness.

Empyema.—In the subacute and chronic types of tuberculous bronchopneumonia, there is found at times an extensive area on one side of the chest showing flatness to percussion, and diminution of the intensity of the respiratory murmur, vocal resonance, and tactile fremitus. The character of the breathing is always bronchial, but so it may be in empyema. In these cases the differential diagnosis from empyema is sometimes quite difficult. In empyema, with free fluid, the outline of the dull area usually assumes a characteristic curve, which is absent in tuberculous bronchopneumonia. Displace-

ment of the cardiac dulness is an almost constant feature of free fluid in the pleural cavity in children, whether right or left, and this sign is absent in bronchopneumonia. The two conditions can usually be easily differentiated by means of the X-ray. In cases of empyema with encapsulated fluid, these diagnostic points are absent, and the diagnosis cannot be made on the basis of the physical signs alone. The occurrence of a preceding lobar pneumonia points toward empyema. In doubtful cases, the diagnosis can only be made by means of exploratory thoracentesis.

Unresolved Pneumonia.—Most often in lobar pneumonia, but sometimes in common bronchopneumonia, the signs of consolidation in the lungs may persist for a long time. Such cases of unresolved pneumonia may finally become infected by extension of tubercle bacilli from the chronic primary lesions, and may become a tuberculous bronchopneumonia. It is often necessary to decide whether a child with such a chronic persistent area of pulmonary consolidation has tuberculous pneumonia or only unresolved pneumonia. The difficulty is further enhanced by the fact that in simple unresolved pneumonia there is often a long persistence of a febrile reaction with an irregular temperature curve, this being due to continued infection with the influenza bacillus or some other organism.

The recognition of the tuberculous nature of these infections is very uncertain. One must depend largely on other evidences of tuberculosis, such as von Pirquet's test, d'Espine's sign, and so forth. When after a pneumonia the temperature falls to normal, and remains normal for a period before going up again, tuberculous infection is suggested. Whenever the area or areas of consolidation, instead of remaining stationary, or diminishing, tend to *increase in size*, tuberculous bronchopneumonia is strongly suggested. Nevertheless, many cases of unresolved pneumonia are wrongly diagnosed as tuberculous, and finally show complete resolution. We should never diagnose as tuberculous, cases showing consolidation with a constantly normal temperature.

Phthisis.—The distinction between chronic pulmonary tuberculosis, and chronic tuberculous bronchopneumonia is based wholly on pathological anatomy. The diagnosis between the two conditions is usually impossible clinically, and is not essential either to prognosis or treatment. If the physician wishes to be corroborated by the report of the pathologist, he will be safer if he diagnoses all cases of chronic tuberculosis with pulmonary consolidation occurring in infants and young children as tuberculous bronchopneumonia. In late childhood, especially with copious expectoration showing tubercle bacilli, phthisis is more probable.

PROGNOSIS.—Among the secondary manifestations of tubercu-



FIG. 194—Tuberculous bronchopneumonia; roentgenogram



losis, tuberculous bronchopneumonia ranks second in fatality to acute miliary tuberculosis and tuberculous meningitis. The acute type is almost invariably fatal. In the subacute type the great majority of cases have a progressive decline, and end fatally, but in a certain number of cases, the progress of the disease is arrested, and chronic fibroid changes in the tuberculous areas eventually lead to full recovery. This improvement may occur at any stage, and the prognosis is not much influenced by the physical signs in the chest. In the chronic type, with proper treatment, there is a great capacity for improvement and recovery, even if extensive consolidation has developed. Some chronic cases die from progressive cachexia, while others eventually become exhausted by repeated attacks, or succumb to a more acute attack. Still, in the chronic type properly treated, the chances are rather in favor of recovery, being the better the older the child.

While in general in tuberculous bronchopneumonia the prognosis is grave, an absolutely unfavorable prognosis should never be given. There is always a possibility of recovery, and this possibility is strengthened the older the child, and the more chronic the disease.

TREATMENT.—The treatment of tuberculous bronchopneumonia is that of any active form of tuberculosis. The essential is fresh air, and cases should if possible have a thorough outdoor treatment, or at least, be kept in a room with well-opened windows. The rest of the treatment is careful feeding, managed like that of other sick children. (See Div. VII, Section on Tuberculosis). Cough rarely is severe enough to demand treatment. Steam inhalations should not be employed, and an opiate given for cough only when absolutely necessary to conserve the patient's strength.

INFLUENZA BRONCHOPNEUMONIA

The bacillus of influenza is frequently found as one of the organisms in the mixed infection of common secondary bronchopneumonia. Its persistence in the lesions of either broncho- or lobar pneumonia is responsible for some cases of long unresolved consolidation with fever. There is a type, however, in which the bacillus of influenza is probably the primary infecting microorganism, and is chiefly responsible for the lesions and clinical manifestations. This type is rarely seen except in widespread epidemics of influenza, but at such times is fairly common. There were a large number of these cases in the Children's Hospital in Boston in 1903, but the type has not been very prevalent here since then. It is to this type that the term influenza bronchopneumonia is applied.

PATHOLOGICAL ANATOMY.—In this form of bronchopneumonia the disease does not diffusely involve a large number of bronchi

of a certain size, but picks out certain bronchi with all their terminal ramifications. Various bronchi are picked out in turn. The bronchus affected, with its terminal bronchioles, and the surrounding alveoli rapidly become filled with a *purulent* exudate, consisting mainly in polynuclear leucocytes. In a few days, the exudate is absorbed, but in the meantime another bronchus is attacked. Sometimes a certain amount of interstitial lung tissue is involved in the suppurative process, and is destroyed, forming a small abscess, which is later healed by fibrous tissue growth. Occasionally a whole area of consolidation becomes gangrenous, softens, and is thrown off in the sputum, being later repaired in the same way.

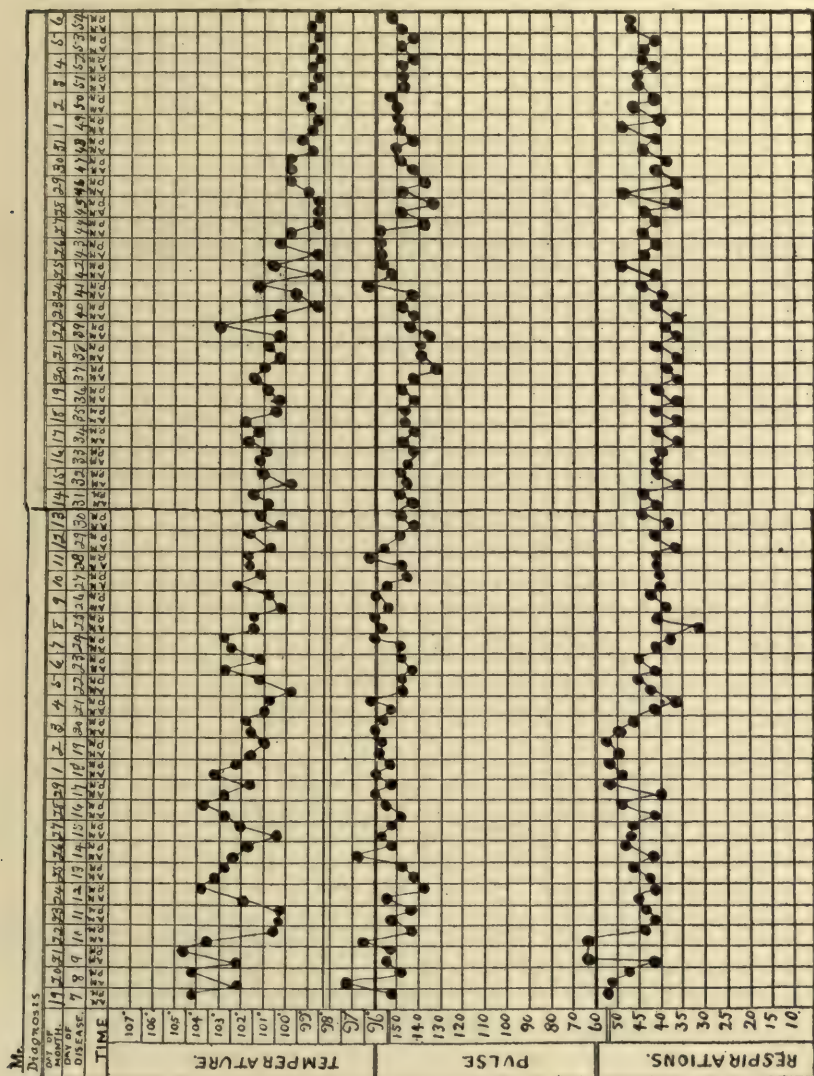
SYMPTOMS.—The onset of the influenzal infection occurs as described in the section on influenza, with high fever, marked constitutional disturbance, and signs of localization in some part of the respiratory tract, such as rhinitis, pharyngitis, laryngitis, or bronchitis. The symptoms of bronchopneumonia come on more gradually. Cough and fever being present already, attention is attracted by increase in the rapidity of the respiration. The respiration reaches 40 to 80 per minute. It is usually not very labored, but slight cyanosis is sometimes present. The temperature continues to be high. The pulse is increased in proportion to the fever. Mental dulness is not marked.

The physical signs of influenza bronchopneumonia are quite characteristic. The main feature is the *successive appearance and disappearance of definite areas of consolidation in different parts of the chest*. For example, on the first day there will be found in some part of a lobe, an area of slight dulness, crackling râles, and diminished breathing. On the next day this area will show marked dulness, bronchial breathing, and râles. On the third or fourth day, only a collection of râles will be heard over this area and the resonance will be normal. On the next day, the area will be clear. Meantime, a new area starts in some other part of the chest, going through the same changes. As the disease progresses, the persistence of each area becomes longer, but the frequency of new areas becomes less, and finally they cease to appear.

The cough in influenza pneumonia is loose, and often paroxysmal, and the sputum is very abundant. In older children there is a profuse, purulent expectoration. Younger children expectorate oftener in influenza pneumonia than in any other form, as if the sputum were so abundant that they cannot swallow it all. Microscopic examination of the sputum shows immense numbers of influenza bacilli, both free, and within the leucocytes. Large phagocytic cells stuffed with influenza bacilli are frequently seen. Sometimes the sputum has a very foul odor, and elastic fibres may

be found microscopically. This means pulmonary abscess or gangrene, which are not infrequent complications.

The course is long, averaging six to eight weeks of fever. The constitutional disturbance which attends the beginning of an influenzal infection does not last more than a week or ten days. During this



There are undoubtedly other clinical types of bronchopneumonia which occur in epidemics of influenza. The common secondary type is just as likely to occur as the pure type. The above is the only type which I have found at all characteristic.

DIAGNOSIS.—The diagnosis of influenza bronchopneumonia depends mainly on the microscopic examination of the sputum, which shows a very characteristic picture. If an epidemic of influenza is present, it should be suspected as the cause when bronchopneumonia appears. The peculiarly characteristic shifting signs in the chest, are almost absolutely diagnostic when present. The diagnosis is important, on account of its bearing on the prognosis.

PROGNOSIS.—The disease is very seldom fatal except in very young infants. On the other hand, common secondary bronchopneumonia due to a mixed infection frequently occurs as a complication of influenza, and is very fatal. When, however, the clinical type described here as influenza bronchopneumonia is recognized, a favorable prognosis may be given.

TREATMENT.—The treatment of influenza is described under that section. Influenza bronchopneumonia requires no special treatment. Cases should be isolated, on account of the communicability of the disease. The hygienic and symptomatic treatment is the same as in secondary bronchopneumonia.

PRIMARY PNEUMOCOCCUS BRONCHOPNEUMONIA

ETIOLOGY.—This type probably represents a primary infection with the pneumococcus, which for some unknown reason, produces bronchopneumonia and not lobar pneumonia. It is only seen in infants.

PATHOLOGICAL ANATOMY.—The lesions are indistinguishable from those of secondary bronchopneumonia due to a mixed infection. There may be considerable fibrin in the exudate, but probably this is not a constant feature.

SYMPTOMS.—This form has an abrupt onset, in every way resembling that of lobar pneumonia. The temperature curve is high and sustained, and the course has the same length as lobar pneumonia, the disease usually terminating by crisis. The disease resembles lobar pneumonia in every way, except in the physical signs found in the chest.

The physical signs are those of a diffuse bronchopneumonia. Scattered moist crackling, or crepitant rales, and occasionally the appearance of areas with signs of consolidation, make the physical signs indistinguishable from secondary bronchopneumonia.

The microscopic examination of the sputum obtained by the

pharyngeal swab, shows very few microorganisms, the pneumococcus predominating.

DIAGNOSIS.—The diagnosis of this form is based on the coincidence of an onset and course resembling lobar pneumonia and the physical signs of bronchopneumonia. Sometimes, if the signs are not very diffuse, being mainly confined to one part of the lung, the diagnosis may be difficult. X-ray examination will often help in such a case, as the single definite shadow of lobar pneumonia is not seen in bronchopneumonia.

PROGNOSIS.—The prognosis of this infection is much more favorable than that of secondary bronchopneumonia, and is about the same as that of lobar pneumonia in infants. The majority of cases which I have seen have recovered.

TREATMENT.—The treatment is the same as that of lobar pneumonia.

TERMINAL BRONCHOPNEUMONIA

This type has no clinical significance. It includes the bronchopneumonia so often found at autopsies in infants and children dying of various diseases. It is often found in fatal cases of tuberculous meningitis, of acute and chronic gastrointestinal diseases, and similar conditions. It represents a terminal infection, and the streptococcus is usually found in the lesions. Clinically, it is only represented by the sudden rise in temperature, pulse, and respiration, which so often occurs shortly before death. It is rarely diagnosed during life.

FRIEDLANDER'S PNEUMONIA

This represents a distinct etiologic type, due to a pure infection with the bacillus mucosus capsulatus (Friedlander's bacillus). It is rare in children, and I have only seen two cases in patients under thirteen years, one of which was in an infant. The disease has a distinct pathological anatomy, the bronchi and alveoli of one or more areas in the lungs being filled with an exudate consisting mainly in enormous numbers of capsulated bacilli, with some polynuclear leukocytes and red blood corpuscles. The consolidated areas have on section a peculiar light greyish mottling, appearing hard and polished, like some varieties of marble.

Not enough cases have been reported to afford a basis for clinical description. The onset and course of the disease resemble those of an atypical lobar pneumonia. Pseudo-crises and recrudescences are common. The signs are simply those of consolidation, and may be found in only one lobe, or there may be more than one area.

The sputum is characteristic, but there is usually not enough peculiarity about the clinical picture to suggest an unusual type of pneumonia, and owing to the difficulty of obtaining sputum in

children, it is usually not examined. It shows great numbers of capsulated bacilli. In one of my cases the diagnosis was made through an exploratory puncture of the chest for fluid. Fluid was not obtained, but cultures from the needle showed a pure growth of Friedlander's bacillus; in the other case the diagnosis was only made post-mortem.

The prognosis has always been regarded as absolutely fatal, most of the reported cases being in adults. My case in an infant, in which the diagnosis was made by lung puncture, recovered. The disease may be commoner in children than is generally supposed, and may account for some atypical cases diagnosed as lobar pneumonia.

The treatment is that of lobar pneumonia.

LOBAR PNEUMONIA

(Croupous Pneumonia). (Fibrinous Pneumonia.)

Lobar pneumonia is an acute infectious disease showing characteristic lesions in the lungs, caused by the pneumococcus (*Fränkel's diplococcus pneumoniae*). It is probable that in a small number of cases a fibrinous consolidation of the lung may be associated with infection with other microorganisms, but it has been shown that in 90 to 95 per cent of the cases, the pneumococcus is the cause of the disease. Lobar pneumonia therefore, from the point of view of the pulmonary lesion, may be considered a specific infection. Fibrinous pneumonia, however, is not the only manifestation of pneumococcus infection, as the organism may, in other parts of the body, produce acute inflammatory lesions having no specific characteristics.

ETIOLOGY.—PREDISPOSING CAUSES.—Lobar pneumonia may occur at any age. It is commoner in infancy than is generally supposed, although not so common as bronchopneumonia. It is less frequent during the first year than in the second, being commonest between the ages of one and six years. From six to ten years it is more common than in the first year, but after the tenth year, its frequency diminishes greatly.

The season of the year has a marked influence on the incidence of lobar pneumonia. It is commonest in the spring, with winter standing next, and is comparatively rare in summer.

The previous condition of the child has no apparent influence on the liability to lobar pneumonia. The disease occurs fully as often in healthy and robust children as in the weak and delicate. Indeed, the majority of cases are seen in healthy children. Possibly this is to be explained by the hypothesis that healthy children contract lobar pneumonia, whereas, under similar circumstances, delicate children contract bronchopneumonia. Previous disease is not a predisposing cause.

The care and hygienic surroundings have a very notable influence on the occurrence of lobar pneumonia. The disease is much commoner among children who are poorly cared for, and who live under poor conditions. This is to be explained, not on the ground of diminished general resistance, but on the ground of increased exposure to the exciting causes of the disease.

EXCITING CAUSES.—The exciting causes which have been associated with lobar pneumonia are fatigue or exhaustion, the inhalation of irritating particles, and exposure to cold. Of these, the last is the most important. Chilling of the whole, or of a part of the body, is the most frequent recognizable antecedent of any attack. When a child is fatigued, such exposure is still more apt to be followed by infection.

MODE OF INFECTION.—The pneumococcus is a frequent if not a constant inhabitant of the mouths of healthy persons. In lobar pneumonia, although various writers have attempted to prove that the pneumococci gain access to the lungs through the blood stream, their evidence is inconclusive, and it is now most generally admitted that the organisms gain access to the lungs through the air passages. But these facts do not explain why infection occurs at all, why some individuals contract pneumonia and others do not. The mechanism of infection in lobar pneumonia is still a wholly unsolved question, and is a fruitful subject of present-day discussion and research.

Three theories have been advanced to explain the onset of lobar pneumonia. They are, 1, the presence of pneumococci of increased virulence; 2, lowered general resistance of the patient; 3, local diminution of resistance through changes in the respiratory tract.

The first theory, that of the presence of pneumococci of increased virulence, supposes that the normal pneumococci of the mouth are frequently entering the lungs, but are destroyed by the inherent resisting power of the tissues. This resisting power cannot overcome a strain of pneumococcus of high adaptation for the infection of man. Such a theory must necessarily emphasize the element of contagion in the onset of lobar pneumonia, and attributes the presence of virulent pneumococci to direct or indirect contact with a previous case. Little evidence has been brought forward in support of this theory. Dochez and Avery found the common pneumococci of the mouth to belong to avirulent types, while more virulent types were found in the mouths of persons who had been exposed, and in convalescents. On the other hand, Cole has shown that pneumonia may be caused by organisms of low virulence. Further, we have no means of showing that the ordinary pneumococci of the mouth, which may be of low virulence for animals, are also of low virulence for man. Against the importance of virulence in the question of

pneumococcus infection, is the rarity with which lobar pneumonia occurs in epidemics. Also, all hospital experience is against any great degree of contagiousness in lobar pneumonia.

The work of Rosenow, which has been frequently referred to in this book, is of importance in connection with the subject of the mode of infection in lobar pneumonia. Under Rosenow's theory, which was described in detail under rheumatic fever, members of the pneumococcus-streptococcus group inhabiting the cavity of the mouth or throat, particularly the tonsils, may encounter conditions favorable to the acquirement of changed biological reactions and selective tissue affinities. These organisms may thus under certain circumstances acquire the characteristics of pneumococci of increased virulence, and a selective tissue affinity, which may permit them to invade the lungs and produce the lesions of lobar pneumonia.

As to the second theory, almost nothing is known concerning diminished general resistance, and its importance. It has been shown that habitual users of alcohol are less resistant when infection has already occurred, and there is some experimental evidence to show that animals suddenly chilled are more susceptible to pneumococcus infection than others. On the other hand, the frequency of lobar pneumonia in healthy persons, and the fact that previous disease is not a predisposing cause, are strong arguments against the theory of diminished general resistance.

The third theory, that of local changes in the lungs being the element most important for the occurrence of infection, is interesting and suggestive. It is well known that thoracic trauma may be followed by pneumonia. It is possible that chilling may produce a congestion of the lung, and even exudation, before the entrance of the pneumococci occurs. Thus anatomical conditions may be produced, highly favorable to the development of the pneumococci of the upper respiratory tract. The study of artificially produced pneumonia in animals, and the course of the disease in man, strongly suggest the possibility of local changes in the living tissue being the chief mechanism by which infection occurs.

It is possible that infection depends on a combination of all three factors. The question is one of the important unsettled problems in medicine, and further knowledge is essential, if any progress is to be made along preventive lines.

COURSE OF THE INFECTION.—The principal localization of the infection in lobar pneumonia, as shown by its characteristic lesion, is the lungs. Nevertheless, the pneumococcus may often be found in cultures from the blood of pneumonia patients, and the frequency of the finding has led some writers to regard pneumococcus infection as essentially a septicemia, with the pulmonary lesion simply a local manifestation of a general infection. It is true, not only that

pneumococci are often found in the blood in lobar pneumonia, but also that cases sometimes occur in which the pulmonary lesion is not prominent, the septicemia dominating the disease picture. Nevertheless, I believe it to be a sounder view that the chief disease process produced by the pneumococcus is the pneumonia, and that septicemia is a secondary manifestation. The pneumococcus cannot be found in the blood in all cases. The percentage of positive findings vary with different observers. The highest percentage obtained in this country has been 91 per cent (Rosenow). Dochez obtained 50 per cent and Cole 30 per cent of positive cultures. Cole believes that the pneumococcus is only found in the blood in the severer cases. Invasion of the blood is rare in children.

The most probable view as to the course of pneumonic infection, is that the lung is usually the primary focus of infection. The inflammation and lesion is a defensive reaction, designed to limit the spread of the infection. When this mechanism is defective, or when the pneumococci manifest a very high virulence, invasion of the blood occurs.

The pneumococci may at times cause secondary local lesions in other organs, which they reach, either by direct extension from the lung to adjacent tissues, or through the blood and lymph channels.

Lobar pneumonia is a self limited disease. If death does not occur, the patient develops an increased capacity for resistance, and this immunity arrests the progress of the infection. The suddenness with which this sometimes occurs in lobar pneumonia is the most striking and dramatic feature of the disease. The nature of the immunity developed in pneumococcus infection will be discussed under the heading of Problems and Research.

PATHOLOGICAL ANATOMY.—The essential lesion in lobar pneumonia is a fibrinous exudate into the alveoli and bronchioles. The exudate contains numerous polynuclear leukocytes, and some endothelial leukocytes, lymphocytes, red blood corpuscles, and serum. In the spread of the exudate, the alveoli are filled before the bronchioles, and in the affected areas all the alveoli are involved. The exudate produces a consolidation, which passes through the stages of congestion, red hepatization, grey hepatization, and resolution. The lesion in children is precisely like that of adults, and requires no detailed description.

The consolidation usually involves part or whole of a single lobe. Much less commonly more than one lobe in the same or different lungs are involved; very rarely an entire lung is solidified. The two lungs are involved with about equal frequency, and the order of frequency in the various lobes is first, the left lower; second, the right upper; third, the right lower; fourth, the left upper; fifth, the right middle.

The inflammatory process begins at a definite focus, and spreads more or less rapidly through the lung tissue by continuity of surface, forming a single area of consolidation, which may spread until the process is arrested by the lobar boundaries, or may cease to spread before the entire lobe is involved. It was formerly supposed that the consolidation might at times begin in the central portion of a lobe, which might be involved for some time before the disease reached the surface. This conception of a "central pneumonia" was framed to explain certain peculiarities of physical examination sometimes observed in lobar pneumonia, which are particularly common in infants and children. It was never supported by post-mortem evidence, and the most recent evidence, based on serial roentgenograms of the chest, suggests that in lobar pneumonia the consolidation always begins at the periphery of the lobe, near the pleural surface, and extends both laterally, and inward toward the hilus of the lung. *The term "central pneumonia" should be entirely discarded, as it is probable that no such thing occurs in pneumococcus infection of the lung.* The peculiarities of physical examination so often seen in infants and children are to be explained on other grounds.

Unless death occurs, the consolidation terminates in resolution. The fibrinous exudate and the products of the inflammation become degenerated, and liquefied, and are removed partly by the lymphatics, partly by phagocytic leucocytes, partly by being coughed up through the upper air passages. The period of resolution usually closely follows the cessation of the evidences of active infection; sometimes, however, resolution may not occur until several weeks after deferescence. In rare instances, abscess formation, either multiple small abscesses, or a single large one, may occur in the consolidated area. Gangrene is extremely rare.

The pleura is usually involved in lobar pneumonia. In the majority of cases there is a fibrinous pleurisy, which is usually so slight as not to affect the clinical aspect of the disease. Sometimes fibrinous pleurisy may be so extensive that the physical signs in the chest are much modified, the term "pleuro-pneumonia" being sometimes applied to such cases. At times there may be a serous pleurisy, in which the exudate is either absorbed, or becomes purulent. At other times, the exudate may be purulent from the start.

The lesions in other organs produced by the pneumococcus in the course of pneumonia are all comparatively rare. The pericardium is sometimes involved by continuity of surface, the lesion being either a fibrinous or purulent pericarditis resembling the pleuritic lesions. In rare cases the pneumococcus is carried to the meninges, causing an acute meningitis with a copious exudate of fibrin and pus. Occasionally peritonitis, arthritis, and parotitis are seen as rare complications.

The kidneys are frequently affected in lobar pneumonia, not by direct invasion with pneumococci, but by the toxins of the disease. The commonest lesion is degenerative, mainly involving the tubules.

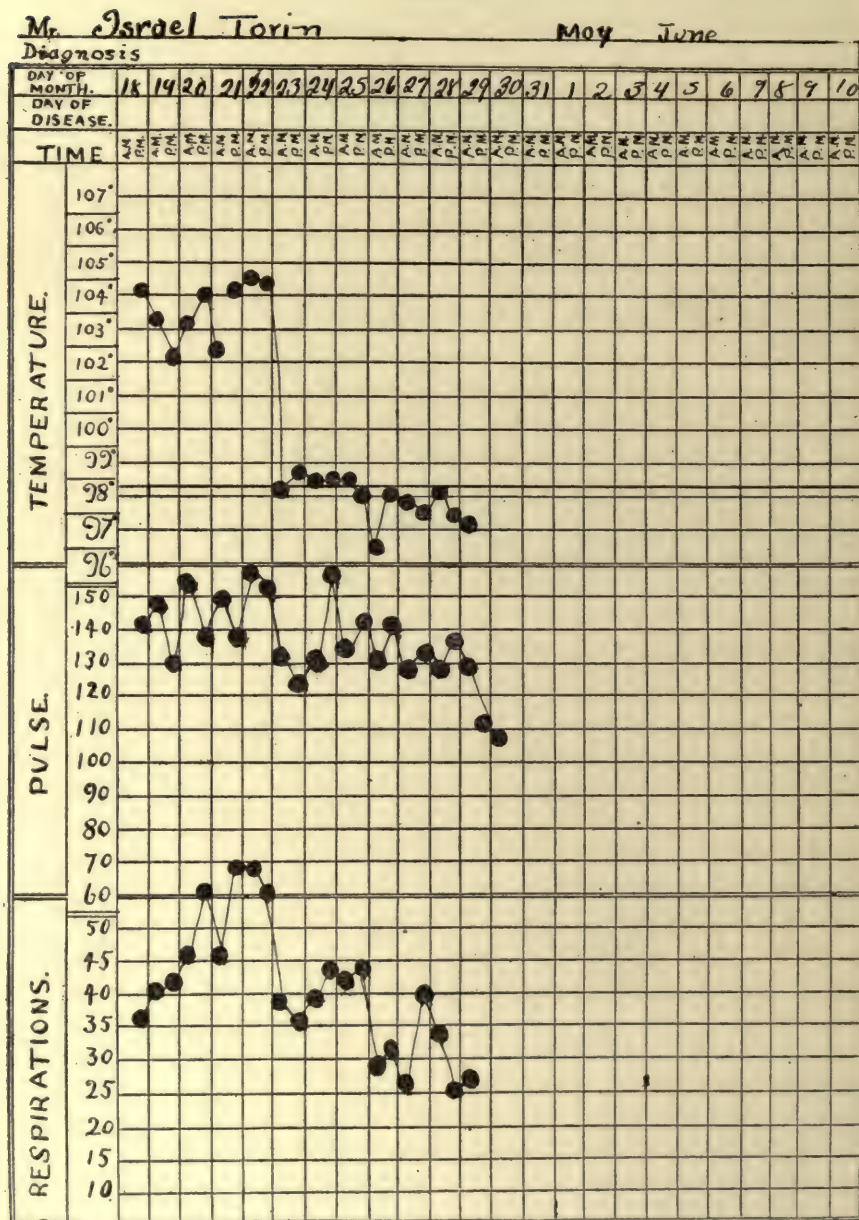
SYMPTOMS. TYPICAL COURSE.—In an infant or young child, after a few hours of slight indisposition, fever develops. The fever may be preceded by vomiting. The child is dull and heavy, and is apt to refuse food, and at times cries out or whimpers as if in pain. Older children often complain of headache, or of pain which they are likely to refer to the abdomen. The thirst, dry skin, and restlessness, which usually accompany fever are present. The temperature is usually between 103° and 105° F., and the pulse 120 to 160. The respiration is notably accelerated, bearing a ratio of 1 to 3 or 1 to 2 to the pulse. Cough is usually absent on the first day.

On the second day, the child is no better; all the symptoms continue, and slight cough usually develops. After this the patient becomes more comfortable; there is less evidence of pain or discomfort, sleep is better, the main symptoms being continued fever, rapid respirations, apathy, and cough. These symptoms continue with little change until the sixth or seventh day, when a sudden improvement occurs. There is less fever, and the temperature falls rapidly to normal or subnormal. With the fall of temperature, the pulse and respirations also drop, and return a little more slowly to the normal. The appetite soon returns, and convalescence is rapid.

THE ONSET.—The onset of lobar pneumonia, while acute and rapid, is less violent and stormy than would appear from the usual descriptions. This is particularly true in infants. In older children the onset is sometimes more stormy, with a chill or chilly sensations, prostration, and severe pain. In infants and young children a chill is practically never seen. Convulsions, which are stated by some writers to replace the chill, are very rare. Cough is slight or absent. Vomiting is comparatively common. The main features of the onset are high fever, accompanied by apathy or drowsiness.

TEMPERATURE.—The temperature rises rapidly, and remains high, 103° to 105° F. In infants, a temperature over 105° F. is not uncommon. It is not so regularly sustained as in adults, remissions of one or two degrees being common; in infants still greater remissions, of three to five degrees are often seen. These remissions are most marked in the early, and again in the last days of the febrile period. The average duration of the fever is, as in adults, six or seven days. A shorter duration is often seen, especially in infants. In fatal cases the average duration is somewhat longer than in those which recover. Toward the end of the febrile period, especially in infants, the remissions may amount to pseudocrises. Although crisis occurs in more than half the cases, the fever terminates less frequently

CHART 23



F. H. Thomas Co., 727 Boylston St., Boston.

Typical Chart of Lobar Pneumonia

by crisis in infants than in older children, this being especially true in the first year. Lysis is usually fairly rapid, and is apt to be slower in cases of long duration.

PULSE.—The pulse is full and bounding at first, and accelerated, averaging between 150 and 170 in infants, and 120 to 140 in older children. As the disease progresses it becomes less full, but serious disturbance of the circulation from the toxemia of the disease, as shown by small, rapid, irregular, intermitting, or dicrotic pulse, is seen much less often than in adults.

RESPIRATION.—The respiration is always accelerated, the average rate being between 50 and 80. In older children it may be below 50, and in infants, it may be over 80. The ratio of the respiratory rate to the pulse rate is always disturbed, and this constitutes the only clinical feature which definitely points to the lungs as the seat of the disease. The proportion is at least 1 to 3, and may even be as great as 1 to 2. The breathing is often accompanied by an expiratory catch, grunt or groan, which is a fairly common and characteristic symptom. The breathing is usually not notably labored with movement of the accessory muscles of respiration, but is shallow and suppressed. Movement of the alae nasi is often present, but may be absent, and is not pathognomonic, nor is it so characteristic as is the expiratory catch or groan.

COUGH.—Cough is often absent at the onset, but usually develops in the course of the disease. It is seldom a prominent symptom in infants, and usually does not attract attention unless the infant is disturbed. In older children, cough is a more noticeable symptom, and is often painful. There is rarely any expectoration until the later years of childhood are reached, and consequently the "rusty sputum" so characteristic of pneumonia in adults is rarely seen.

PAIN.—Pain is a difficult symptom to estimate in infants, but, so far as can be judged by their actions, is often present. It is shown by whimpering or crying when the infants are disturbed, or by their keeping very quiet with a frowning expression of face. In older children pain is often a prominent symptom. It is frequently referred to the abdomen, particularly in the early part of the attack. Later it may be referred to the side of the chest, and is increased by deep respiration or coughing.

THE DIGESTIVE TRACT.—This is usually more or less disturbed in lobar pneumonia. Anorexia is usually very marked, and the tongue is dry and coated. Vomiting is not very common after the onset, but diarrhea is often seen in infants, and may be serious. Constipation is much less common, and is most often seen in older children. Abdominal distention is frequently seen in infants, and

may be a symptom of grave import, difficult to relieve and hastening a fatal termination.

NERVOUS SYSTEM.—The nervous system is always more or less affected by the toxemia of the disease. The usual mental condition is one of apathy or drowsiness. I have occasionally seen delirium or evidences of cerebral excitement in infants, but this is unusual. In middle and late childhood, delirium at night is much more common, and while usually there is only a mild wandering, in severer cases there may be marked cerebral excitement, with continual movement of the head, muscular twitchings, rigidity of the neck and upper extremities, retraction of the head, and Kernig's sign. These

FIG. 195



Lobar pneumonia. Female, 8 years old. The part of the lung involved by the pneumonic process is shown by black lines, and the area of diminished resonance and the fine râles are marked by black spots.

symptoms usually occur comparatively early in the course of the disease, and while they are strongly suggestive of meningitis, they are usually not due to meningitis, but are due to cerebral irritation from the toxin of the disease. An actual meningitis may develop as a complication of pneumonia, but is rare, and when it does occur, it usually develops late. Functional disturbance suggesting meningitis, however, is not uncommon, and may counterfeit a true meningitis in every important respect.

THE SKIN.—Flushing of the cheeks is uncommon in infants and young children, and has no diagnostic value either as to the presence

of pneumonia or as to its location. Cyanosis is not seen except in exceptionally severe cases. Pallor is common, especially in the severer cases. Herpes labialis is unusual in children.

THE URINE.—Most textbooks agree that the kidneys are rarely involved in lobar pneumonia. These statements are probably based on the examinations of the urines of older children. The urine is always scanty, high-colored, concentrated, loaded with urates, and with a marked diminution of chlorides. Albumin and casts are rarely seen in older children, but in infants are quite common.

FIG. 196



Lobar pneumonia. Three invasions. Male, 6 years old

THE BLOOD.—Leukocytosis is the rule in children as in adults, varying from 20,000 to 50,000. The increase is chiefly in the polymorphonuclear cells. The behavior of the leukocyte count is of no value in prognosis.

PHYSICAL EXAMINATION. THE LUNGS.—The signs in the chest in childhood are in their general characteristics the same as in the adult, namely dulness, bronchial breathing, bronchial voice sounds, and crepitant râles, confined to a single lobe of the lungs. In some cases, especially in later childhood, but occasionally in infants, the signs in the lungs are exactly like those in adults.

Usually, however, there are certain differences between the physical signs of children and adults, which differences are more marked the younger the patients. The principal differences in childhood are the following: 1, the signs are very often late in appearing; 2, the respiration even though bronchial in quality, is apt to be diminished in intensity; 3, prolonged expiration is often not noticeable, even when the breathing is bronchial in quality. As to the first difference, there is no rule for the time when the physician first detects signs of consolidation in the chest. Signs may develop just after the onset, or, in extreme cases, may not be found till the day of the crisis. The diminution in the intensity of the respiration on auscultation is very important. The breathing and voice sounds are usually diminished during the first few days after the development of signs, and often remain less loud than on the unaffected side of the chest throughout the course of the disease; sometimes they become loud toward the end. The physician must learn to recognize bronchial breathing in children entirely by its quality, as it cannot be properly described; no text-book description is adequate. He cannot rely on prolongation of the expiration, as this is often not notable in children, or the expiration is replaced by a grunt or cry. He must judge mainly by the peculiar high pitched, tubular quality of the respiration, which, even though very faint, seems to come from a point intermediate between the ear and the chest wall. The normal breathing of infants and young children is loud and harsh. The breathing heard over a consolidation in infants and young children is usually less loud, and is never harsh, and often resembles the normal breathing of adults, the bronchial quality only coming out when the infant cries or draws a deeper breath. Whenever there is a difference between the two sides, and doubt as to the interpretation of the signs, it is usually correct to consider the louder harsher side the normal, and the fainter side the consolidated. Of course loud breathing is sometimes heard over a consolidation, but in such a case its bronchial character is unmistakable.

The first sign usually noted is an area in one lobe where the intensity of the respiration is diminished as compared with the rest of the chest. The next step is the appearance of slight dulness to percussion over this area, which may also have a slightly tympanitic character. At some time during this early stage, fine crepitant râles may be heard over the suspicious area, coming usually at the end of inspiration. These râles when heard are a great aid in diagnosis, but they are often only present for a short time, and may be missed.

In the next stage dulness becomes more marked, although flatness is rare, unless there is an extensive accompanying pleurisy. The respiration over the dull area remains diminished in intensity, and gradually assumes a slight bronchial character. In this stage the



FIG. 197—Lobar pneumonia. Showing area involved in upper lobe consolidation from in front.



FIG. 198—Lobar pneumonia. Showing area involved in upper lobe consolidation from behind.



FIG. 109.—Lobar pneumonia. Showing area involved in lower lobe consolidation from in front.



FIG. 200.—Lobar pneumonia, Showing area involved in lower lobe consolidation from behind.



FIG. 201—Lobar pneumonia.
Showing area involved in consolidation of the middle lobe.

vocal resonance and tactile fremitus may be increased in intensity or they may be diminished; the latter is found when there is much pleurisy. Finally there appears in some part of the dull area a definitely circumscribed spot, in which the bronchial character of the breathing is quite manifest. Even in this stage, the breathing usually remains diminished in intensity. These signs may last until recovery or death takes place, or the area of bronchial breathing may spread all over the dull area, finally becoming loud, and resembling the bronchial breathing of the adult.

These changes may take place rapidly or slowly. They may, especially in older children, reach full development early, or, especially in infants, they may not reach it till the day of the crisis. After the crisis or beginning of lysis, resolution begins, and the signs of consolidation disappear, either rapidly or slowly. The pure bronchial breathing becomes broncho-vesicular, and finally vesicular. Meanwhile moist râles of all kinds appear over the dull area. Very slight dulness, and slightly diminished respiration may persist for some time.

The signs are usually confined to one lobe, and may involve all or part of a lobe. In rare cases there may be consolidation in another lobe. In the lower lobes, bronchial breathing most often appears first near the angle of the scapula. In the upper lobes, the most important point to auscult for bronchial breathing is not below or above the clavicle in front, but either near the posterior axillary fold, or in the apex of the axilla.

The differences in the physical signs in the chest in children and adults are best explained by the peculiar anatomy of the lungs in early life. In young children the proportion of alveolar air space to bronchial air space is much less than in adults, and it is the greater proportion of bronchioles which gives to normal puerile breathing its loud harsh quality. The pouring out of exudate causes a diminution of this loud harsh quality, and the breathing becomes relatively diminished in intensity. Bronchial breathing is caused by the transmission of the sounds from the trachea and primary bronchi through a solidified area. Air-containing tissue interferes with such transmission. There is often a delay in the extension of the solidified area from the surface to the region of the hilus, and consequently a delay in the transmission of the bronchial breathing. Furthermore, in children, the transmission of bronchial breathing is less perfect than in adults, as the medium-sized bronchi do not fill with exudate, and, being in greater proportion to the alveoli, interfere with transmission. Only when they fill with exudate is the transmission of bronchial breathing perfect in children, and they either do not fill at all, or fill only as resolution is approached.

Occasionally there may be noted a limitation of the excursion of the chest wall on the affected side. Often, during the height of the

consolidation the resonance of the unaffected portions of the chest is exaggerated and even tympanitic. The breathing and voice sounds are often louder over the healthy lung than they were before consolidation occurred. Pleuritic friction rubs are sometimes heard, especially during and even after resolution.

VARIATIONS IN TYPE. ABORTIVE.—In both infancy and childhood it is not uncommon for the course of lobar pneumonia to be shorter than the average. The crisis may occur from the third to the fifth day in these cases. A type almost peculiar to the first two years is the "abortive." The onset is the same as in the usual type, and diminished breathing with slight dulness, may appear in the lung. After twenty-four to forty-eight hours however, the temperature falls, usually by crisis, and the lungs clear rapidly.

PROLONGED TYPE.—Prolonged cases are also not unusual, especially in infancy. Sometimes the temperature continues, with exacerbations and remissions, for a varying period which may reach the tenth or fourteenth day, or even later. During this time in some cases there is no change in the physical signs to account for the continuance of fever. In other cases there is either evidence of extension of the consolidation in the same lobe, or evidence of fresh consolidation in some other lobe. Pseudocrises are common in these prolonged cases. It is not known whether they represent continued activity of the pneumococcus infection, or a mixed infection. Empyema is always suggested in these cases and can only be excluded by repeated careful examinations of the chest. Sometimes the temperature goes up after a period of normal temperature. This also may be due to reinfection in some other lobe, or it may be due to empyema or some other complication.

In some cases, the fall of temperature in lobar pneumonia is not followed by resolution. The temperature remains normal, but the signs of consolidation in the lungs persist for an indefinite period. In most of these cases of "*unresolved pneumonia*," resolution eventually occurs. Unresolved pneumonia is rare in early life, and is more often seen in bronchopneumonia than in lobar pneumonia. Rarely the unresolved area may become the seat of secondary tuberculous infection, which is shown by the reappearance of irregular fever, and a gradual change in the physical signs.

SEVERE TYPE.—As compared with the disease in adults, lobar pneumonia in children is a very mild disease. Severe toxemia, with circulatory failure, is comparatively rare. Nevertheless, at times severe cases occur, in which there is a pronounced nervous disturbance, or symptoms of circulatory or respiratory failure.

The signs of circulatory failure are cold extremities, pallor, muscular weakness, and a pulse which is rapid, compressible, and sometimes

irregular. The signs of respiratory failure are very rapid and superficial breathing, cyanosis, and loud tracheal râles.

Death may occur early in the disease, when the consolidation is widespread, involving more than one lobe. In most uncomplicated fatal cases, it occurs toward the time when the crisis is expected, the usual cause being circulatory failure. A fatal ending is more apt to occur when some complication develops.

ABDOMINAL TYPE.—The thoracic pain due to the pleurisy which accompanies lobar pneumonia is in childhood often referred to the abdomen. When the diaphragmatic pleura is involved, there may be, in addition to abdominal pain, marked tenderness on palpation of the abdomen, and even muscular rigidity. Vomiting is most common, also, in these cases. The abdominal symptoms may be so pronounced as to dominate the clinical picture, and suggest appendicitis, and if signs of consolidation have not yet appeared in the lungs, the diagnosis may be difficult.

CEREBRAL TYPE.—In some cases, the symptoms of disturbance of the nervous system may dominate the clinical picture. Severe headache, vomiting, rigidity and tenderness of the neck, retraction of the head, rigidity and twitchings of the extremities, Kernig's sign, active delirium—all these symptoms may be present, and the disease may simulate an acute meningitis.

PLEURO-PNEUMONIA.—In some cases there is an excessive amount of fibrinous pleurisy, in which often pockets of pus are formed. In general these cases resemble in their course the severe type described above, with marked constitutional disturbance. The main peculiarity is in the physical signs, which are markedly affected by the extensive pleurisy. In the early stage pleuritic friction rubs are very prominent, and persist after signs of consolidation appear. The signs of consolidation may be masked by the pleurisy. There is usually marked dulness, or even flatness. Bronchial breathing is distant, and vocal resonance and tactile fremitus are markedly diminished. The signs may be strongly suggestive of pleuritic effusion. This type is very fatal in children under two years.

COMPLICATIONS.—*Otitis Media* is by far the most common complication seen in lobar pneumonia. It occurred in 18 per cent of Morse's series. In the cases during my series at the Infant's Hospital, in which routine examinations of the ears were made on every case, the percentage was much higher than this.

Empyema is the most important complication. A certain amount of pleurisy probably accompanies every case of pneumonia, which pleurisy is usually of the dry fibrinous form. Empyema is most common in the type described above as pleuropneumonia, as the excessive fibrinous pleurisy usually contains pockets of pus, which

develop into empyema. Serous effusion is unusual, and when it does occur, it usually becomes purulent. Empyema occurred in 8 per cent of Morse's Infants' Hospital series. It may develop either during the course of the pneumonia, or during the first few days after the crisis.

Nephritis sometime occurs in lobar pneumonia, particularly in infancy. Its occurrence is often overlooked, owing to the trouble of obtaining specimens of urine in infancy.

Pericarditis, although a very uncommon complication of pneumonia, is more often seen in children than in adults. When it occurs, it usually complicates the pleuro-pneumonia type, and develops during the height of the disease. The exudate is fibrino-purulent. It is usually discovered by physical examination, rarely giving rise to new symptoms.

Gangrene and *abscess* of the lung have been seen in lobar pneumonia, but are very rare in early life.

Meningitis due to the pneumococcus is a rare complication of pneumonia in early life. It usually occurs late in the course of the disease.

Endocarditis, *Peritonitis*, *Parotitis*, and *Arthritis*, have all been noted as complications of pneumonia, but are quite rare.

DIAGNOSIS.—In the early stages of lobar pneumonia there is in children a variable period before any physical signs appear in the chest. The onset of lobar pneumonia resembles that of any acute general infection, and the symptoms do not point unmistakably to the chest. Consequently lobar pneumonia in this stage must be distinguished from a number of infections of acute onset, with fever.

Influenza, *scarlet fever*, *tonsillitis*, *gastro-intestinal infection*, *pyelitis*, *otitis media*, *typhoid fever*, and *malaria* have all presented difficulty in differential diagnosis from pneumonia in the beginning of the attack. In general, at this stage, the diagnosis of lobar pneumonia rests chiefly on the character of the respiration. Rapid breathing with a ratio to the pulse of 1 to 3 or more, is strongly suggestive of lobar pneumonia. In every case three things may be present. First, the respiration may be so rapid and characteristic as to make the diagnosis of pneumonia practically certain. Second, the respiration may be so little increased in rate, as to enable one at once to exclude pneumonia. Third, the respiration may be accelerated enough to be compatible with pneumonia, but not enough to make the diagnosis certain. With this third possibility there may be some difficulty in diagnosis, as in the onset of some other acute infections, notably pyelitis, the respiration may be considerably accelerated. Whenever in addition to being rapid, the respiration is pneumonic in character, with an expiratory catch or grunt, and when cough is present, the



FIG. 202.—Lobar pneumonia. Roentgenogram taken before the appearance of physical signs. The plate shows consolidation beginning at the periphery of the right upper lobe.

diagnosis of pneumonia may usually be made. Rigidity of the neck and upper extremities without rigidity of the lower extremities is a valuable confirmatory sign at this stage. The differential diagnosis between *meningitis* and lobar pneumonia with meningeal symptoms has been discussed under epidemic cerebrospinal meningitis.

Many of the other acute infections of which the onset may suggest pneumonia, present early signs which are of value in diagnosis. Influenza usually shows some catarrhal inflammation of the upper air passages. In scarlet fever and tonsillitis, sore throat is usually prominent, and examination of the throat reveals a characteristic appearance. Gastro-intestinal infection gives usually a more severe and characteristic diarrhea than does pneumonia, and the respiration is almost never accelerated. Pyelitis, in my experience, is often mistaken for pneumonia, but can easily be recognized if the urine be examined. Otitis media is only overlooked because the ears are not examined. Typhoid fever and malaria only occasionally have an onset acute enough to resemble pneumonia, and can be recognized if a blood count be made, by the absence of leukocytosis.

After the signs appear in the lungs, the diagnosis of lobar pneumonia is often easily made, but at times there is difficulty in differentiating it from *bronchopneumonia*, *pleurisy with effusion*, and *tuberculosis*.

Bronchopneumonia.—In lobar pneumonia the disease is usually evidently primary with an acute onset; in bronchopneumonia the disease is usually secondary with a slower onset. In the early stage of lobar pneumonia, either no signs are found in the chest, or there are signs in a definite area in one lobe; in bronchopneumonia, some signs in the chest are present from the beginning, and they are usually not confined to one lobe, but involve both lungs. In lobar pneumonia the consolidated area is sharply defined, and râles are heard only over it, and then only in the early stage and during resolution, unless there is a complicating bronchitis; in bronchopneumonia the consolidated areas are indefinite in extent and distribution, and râles are heard in other parts of the chest as well as over the dull areas, and are to be heard throughout the disease. In lobar pneumonia there is a fairly regular course, frequently terminating by crisis within a week; in bronchopneumonia the course is irregular, the temperature more remittent, the duration longer and more indefinite, and the termination is by gradual lysis. In lobar pneumonia resolution is rapid, usually being complete within a week; in bronchopneumonia resolution is often slow and incomplete.

The roentgen ray will often clear up the diagnosis better than can physical examination.

Pleuritic Effusion.—In the early stages of lobar pneumonia, the signs do not markedly suggest pleuritic effusion. Late in the course

of the disease, when the signs of the consolidation have become marked throughout an entire lower lobe, or when the pleuropneumonic type exists, the diagnosis is more difficult.

It is often important, even when pneumonia is known to be present, to determine if pleuritic exudation has occurred. The differentiation of an unresolved pneumonia from empyema is particularly difficult in certain cases, being much more difficult than in adults. The signs obtained on auscultation are often of little value in childhood, because in both diseases there is often diminished bronchial breathing, bronchophony, and diminished vocal resonance. Of course, if there is loud bronchial breathing, with increased vocal resonance and tactile fremitus, the evidence points toward pneumonia without pleuritic effusion, but these signs are often absent in pneumonia. Râles point toward pneumonia, but they may often be heard through a pleuritic effusion.

The differential diagnosis of these two conditions rests mainly on these three points: 1, the character of the dullness; 2, the outline of the dullness; 3, displacement of the heart. These points will be discussed in greater detail under pleurisy. In pleuritic exudation, the area is more apt to be flat than merely dull; there is a sense of wooden resistance not often felt in simple consolidation. In lobar pneumonia, the dull area is either within one lobe, or is confined to the boundaries of one lobe, and when the lower lobe is involved, the outline of dullness extends downward in the axilla and does not rise high in front. In pleurisy with free fluid, the outline of dullness assumes a fairly typical "S" curve, and rises high in front, as high as it does behind. Flatness over an entire lung points toward fluid. Displacement of the heart in children occurs with much less fluid than in adults, and is a very constant sign of effusion, whether the fluid be on the right or on the left. If this sign is definitely established, fluid is surely present. If it be absent, the presence of fluid is improbable, but is not positively excluded.

This differential diagnosis applies only to cases of pleurisy with effusion in which the fluid is free. If an empyema be encapsulated, a differential diagnosis can often only be made by exploratory puncture.

Roentgen ray examination of the chest is often of great value in distinguishing between fluid and consolidation.

Tuberculosis.—The form of tuberculosis which in children might resemble lobar pneumonia in its physical signs, is tuberculous bronchopneumonia. It can usually be recognized by the entirely different history of the onset and course of the disease.

There are two variations in the type of lobar pneumonia which often complicate the diagnosis; these types suggest *meningitis*, or *appendicitis*.



FIG. 203.—Lobar pneumonia. In this case physical examination showed dullness and diminished breathing over the entire right chest. The plate excludes pleuritic effusion, and shows consolidation of the upper and middle lobes. This was confirmed at autopsy; there was a fibrinous pleurisy over the lower lobe.

Meningitis.—All the clinical symptoms and signs of meningitis may be present in the lobar pneumonia of early life without there being any actual infection of the meninges. The meningeal symptoms are due to a condition sometimes spoken of as “meningismus,” in which the nerve cells of the central nervous system may be irritated by the pneumococcus toxins, causing sensory and motor nervous manifestations, or the meninges may be irritated, causing increased formation of cerebrospinal fluid. In pneumonia, *these meningeal symptoms usually occur early in the course of the disease.* They can only be positively recognized as being due to meningismus, by the results of lumbar puncture. When, with meningeal symptoms occurring early in an acute infection, signs of consolidation are found in the lungs, the physician is justified in attributing the meningeal symptoms to lobar pneumonia, and lumbar puncture is not indicated. If, early in the course of the attack, meningeal symptoms are pronounced, and signs of consolidation cannot be found in the lungs, lumbar puncture is indicated to determine if the infection is meningitis or pneumonia. In a case already recognized as pneumonia, with signs of consolidation in the lungs, if meningeal symptoms develop late in the course of the disease, lumbar puncture is indicated to determine if meningitis has developed as a complication.

Appendicitis.—Appendicitis is sometimes suggested in cases of pneumonia in children in which there is pain referred to the abdomen, abdominal tenderness and spasm, and vomiting. Whenever in such cases definite signs are found in the lungs on auscultation and percussion, it is generally safe to attribute the abdominal symptoms to lobar pneumonia. Difficulty in diagnosis is only encountered in cases with abdominal symptoms in which signs have not yet appeared in the lung. The location of the abdominal tenderness is often not of much value in differential diagnosis, as this is often difficult to determine in young children; moreover, in children with appendicitis the tenderness is often higher up than in adults, or is very general. Involuntary muscular spasm points toward appendicitis, but has been seen in pneumonia. If the respiration is accelerated, and of the pneumonic type, the evidence points toward pneumonia; and the rate and character of the respiration is the main point on which the diagnosis rests, in the interval before the appearance of signs of consolidation.

PROGNOSIS.—In children beyond the age of infancy, the prognosis of lobar pneumonia is very favorable, much more so than in adult life. The mortality at this age is in general from 3 to 5 per cent. In general, in a case of lobar pneumonia in middle childhood, the parents may be assured that unless some complication develops, the child will recover, and that complications are comparatively rare.

In infancy, the prognosis is not so favorable. In Morse's analysis of 118 cases, there was a mortality of 31.9 per cent in the first year, 17.9 per cent in the second year, giving an average of 22.8 per cent in the first two years of life. These figures were taken from Infants' Hospital cases, and probably are higher than would occur in infants from the best hygienic surroundings. The death rate in private practice for pneumonia in infancy is probably from 10 to 20 per cent.

Death in lobar pneumonia usually occurs either from the development of some complication, or from very extensive involvement of the lungs. In the latter condition there is probably also a marked invasion of the general circulation with pneumococci, and these cases probably represent either infection with an exceptionally virulent type of pneumococcus, or exceptionally low resistance.

The temperature has less effect on the prognosis than might be expected. A high temperature is the rule, and occasional rises to over 105° F., do not affect the prognosis. When, however, the temperature remains continuously above 105° F., the prognosis is less favorable. When the fever continues beyond the tenth day, it is a rather bad sign, suggesting either a new pneumonic focus, or some complication.

A high rate of pulse and respiration is compatible with recovery, but means a comparatively severe case. A low rate of pulse and respiration means a mild case, with a very favorable prognosis.

Bad signs in lobar pneumonia are the following: 1, extensive consolidation, involving both lungs; 2, signs of extensive pleurisy; 3, prolonged fever; 4, late extension of consolidation to another lobe; 5, nervous symptoms developing late; 6, vomiting, diarrhea, or abdominal distention occurring late; 7, delayed resolution.

TREATMENT.—Lobar pneumonia is a self-limited disease of comparatively short duration, with a strong tendency toward recovery. There is no drug which has given any evidence whatever of any influence on the course of pneumococcus infection. Consequently, the indications are to place the patient under the best hygienic conditions, to treat such symptoms as can be favorably influenced without disadvantage, and to watch for complications. Often in children, even symptomatic treatment is not required, and the routine treatment of the various symptoms of the disease has the disadvantage of disturbing the child, and doing more harm than good. In the majority of cases, hygienic treatment is all that is required. The most careful nursing is essential.

Children with pneumonia should always be kept in bed, no matter how mild the case, and should be disturbed as little as possible. Rest and sleep are essential, and the surroundings of the patient should be kept perfectly quiet. The giving of medicine, and dis-

turbing therapeutic measures, should be avoided, unless the indications are very marked. The bowels must be kept properly open. At the very outset of the attack, a dose of castor oil or calomel may be given. During the course of the disease, a standing order should be left with the nurse to give an enema if the bowels have not moved once in twenty-four hours.

The diet should be that of any acute infection of short duration. Food should be given at regular intervals, not oftener than once in three hours. Anorexia is often very marked in lobar pneumonia, but feeding should not be forced in the early stages of the disease. Late in the disease, or in prolonged cases, forced feeding is sometimes necessary, and in infants, milk sometimes has to be given by gavage. After the first few days, the physician should see that the child takes at least twenty ounces of milk daily. In cases in which an insufficient amount of food is taken, whiskey should be given in doses of from 20 to 30 drops every four hours to a child over one year. Plenty of water should be given at all times.

COLD AIR TREATMENT.—It has long been recognized that plenty of fresh air is of value in the general hygienic management of lobar pneumonia. Recently it has been shown that children with pneumonia do better when the air they breathe is not only fresh, but also *cold*. The importance of cool, fresh air has been most ardently advocated by Northrup, and the majority of authorities in this country have become converts. In my own experience, children with pneumonia who are kept in cold rooms not only sleep better and cough less, but are also less likely to show serious nervous or circulatory disturbance.

Grave symptoms and deaths from pneumonia have long been attributed to failure of the vasomotor mechanism. Howland and Hoobler have shown by blood pressure experiments the effect of cold air. Babies subjected to its influence showed a rise in blood pressure, but when removed to a warm, well-ventilated ward, showed a fall. They attributed this effect to reflex stimulation of the vasomotor centres. More recently doubt has been thrown on the cause of the favorable action of cold air by the experiments of Newburgh and Minot, who came to the conclusion that the blood pressure curve does not suggest the failure of the vasomotor centres in pneumonia, that a low systolic pressure is not an unfavorable sign, and that the blood pressure cannot be taken as a basis for the administration of drugs. Also the physiological experiments of Porter, Newburgh, and Newburgh tended to show that the vasomotor centre is not affected in pneumonia. Nevertheless, these experiments do not contradict the possibility that in pneumonia the blood pressure is only maintained at a given point by unnecessary cardiac exertion,

and that reflex stimulation of the vasomotor centre by cold air may act favorably by lessening the burden on the heart.

In the use of the cold air treatment, children should be kept in a room with the windows wide open. I usually give directions that the temperature in the sick room in winter must not be allowed to rise above 50° F. Of course, in carrying out this treatment, the garments and bed-clothing of the child must be adapted to the temperature of the room, as it is essential that the body of a child breathing cold air be kept comfortably warm. Some sort of hood should cover the head, leaving only the face exposed, and if necessary on very cold days, hot water bottles and extra blankets must be used.

Much prejudice will be encountered in instituting the cold air treatment in private practice, as it runs counter to long established ideas as to the danger of "taking cold." This prejudice is fast lessening in extent, and can often be successfully combatted by tact on the part of the physician. When it cannot be overcome, the physician is constrained to limit his endeavors to seeing that the sick room is as well ventilated as possible.

SYMPTOMATIC TREATMENT.—In the majority of cases of lobar pneumonia in children, no symptomatic treatment is required. The symptoms which occasionally require treatment are *pain, cough, hyperpyrexia, nervous disturbance, and circulatory failure.*

Pain when not severe, is best relieved by an ice-bag. In some children, the ice-bag seems to cause discomfort, and in such a case counterirritation by means of a mustard paste may be tried. At times a tight swathe about the chest will relieve pain. Poultices should not be used. When pain is severe, doses of codein may be given, proportioned to the age of the child.

Cough rarely requires treatment when the cold air routine is used. When it is so severe as to interfere with sleep, codein, or Dover's powder may be used, in doses proportioned to the patient's age.

Hyperpyrexia in lobar pneumonia is common, and does no especial harm. The coal tar antipyretics should not be used to reduce temperature. Hydrotherapy is preferable, but in my experience it usually disturbs children more than it helps. In certain cases in which a very high temperature is accompanied by restlessness or other nervous symptoms, the cold pack, or even a sponge bath may be tried, but should only be continued if the nervous symptoms are helped. Hydrotherapy should never be used as a routine, no matter how high the temperature.

Nervous disturbance in lobar pneumonia should be treated, when it interferes with sleep, or is severe and exhausting. When mild, some mild hypnotic, such as trional or codein may be given at night. When severe, sodium bromide is by far the best drug for use in

children. Cold sponging, and an ice-bag to the head, may be used also. Often tepid sponging will be more effective than if colder water is used.

Circulatory failure is treated in the same way as in bronchopneumonia.

SPECIFIC TREATMENT.—Both vaccine therapy and serum therapy have been recommended in lobar pneumonia. In children, owing to the comparative rarity of severe uncomplicated cases, neither form of specific treatment has been much employed.

As far as vaccine therapy is concerned, there are only a limited number of individual statistical reports in its favor, which are wholly inconclusive. The weight of evidence at present is wholly against any value from vaccine therapy, and the present trend of scientific investigation does not hold out much hope of benefit from its use.

It is very different as regards serum therapy. There is considerable evidence that serum therapy may be of decided value in lobar pneumonia. The final proof is still lacking, and in view of the favorable course of lobar pneumonia in children, there is little occasion for specific treatment. Nevertheless, at the present time, there is great activity in research on immunity and serum therapy in pneumococcus infection. In any very severe case of lobar pneumonia in a child, if any antipneumococcic serum can be obtained, I believe it should be tried. It is probable that within a very short time, there will be great additions to our knowledge of serum therapy in pneumococcus infections. This will be further discussed under Problems and Research.

PROBLEMS AND RESEARCH.—The following problems in lobar pneumonia are now engaging the attention of investigators: 1. The mode of infection; 2. the nature of the toxemia; 3. the nature of the immunity, and the mechanism of the crisis and of resolution; 4. vaccine therapy; 5. serum therapy.

The problems as to the mode of infection have already been discussed under Etiology.

THE NATURE OF THE TOXEMIA.—The symptoms of lobar pneumonia are of such a general character, showing effects of the infection upon such distant organs, that a toxemia is strongly suggested. All attempts, however, to discover a soluble toxin in pneumococcus cultures have failed. Moreover, the serum of rabbits artificially infected, taken just before death, was found non-toxic. This simply shows that the metabolic products of pneumococci *in vivo* are not different from those *in vitro*, but does not show that no toxin is formed in pneumonia, but only emphasizes the difficulty of demonstrating toxin formation *in vitro* and in an animal, in a disease like lobar pneumonia, in which enormous numbers of organisms are needed

to produce death even in the most susceptible animals. In man the amount of toxin present at any one time may be very small, and yet, when acting on tissue-cells for six or seven days, may produce marked effects.

Recent experimental evidence is against the theories, 1, that the symptoms of lobar pneumonia are due to absorption of the products of digestion of the pathological exudate in the lung, 2, that they are due to a disturbance of salt metabolism caused by the pneumococcus, and 3, that they are due to an acidosis produced by the pneumococcus. The study of the oxygen-content of the blood, undertaken to estimate acidosis, has revealed another fact of interest, namely, that in pneumonia the oxygen-carrying power of the blood is diminished through the formation of methemoglobin. While this change possibly plays a part in the fatal termination, it is probably not the only factor, but is an effect of the toxemia.

It is most probable that the symptoms are due to a toxin derived from the bodies of the pneumococci. It has been proved that toxins may be obtained from the pneumococci in various ways, although pneumococci killed by heat have very little toxicity. Opinions differ as to the mode of formation of these toxins. One of the chief topics of discussion at present is whether the toxins obtained from the pneumococcus represent intermediate products of protein digestion formed by ferments from the bodies of the bacteria, or whether they are simply contained within the bacterial bodies in accordance with the well-known endo-toxin theory of Pfeiffer.

THE NATURE OF THE IMMUNITY.—The problem of the nature of the general resistance of the body to the pneumococcus infection is receiving much study. Lobar pneumonia with its sudden crisis, always a startling and dramatic event, would appear to offer an especially favorable opportunity for the study of the process of recovery. One theory suggested is that the crisis represents a kind of anaphylactic reaction, a form of cumulative shock, following which the patient is in a refractory stage. There is no convincing evidence in support of the theory.

The occurrence of recovery in about seven days is strongly suggestive of a true immunity reaction. The attempts to demonstrate the appearance of known immune substances in the blood during and following an attack of pneumonia have not been very successful, and an increase of the ordinary bactericidal substances which act in conjunction with complement has not been proved. There is, however, strong evidence that the leukocytes are concerned in recovery. Several observers have found an increase in the phagocytic activity of the serum after recovery, the activity being usually limited to a homologous strain of pneumococcus. That phagocytosis is concerned

in recovery is probable, but there is certainly not as yet sufficient evidence for the conclusion that recovery is due *merely* to an increase of opsonins.

Of great importance are the recent experiments by a number of observers showing an increased protective power for mice in the blood of patients after recovery from pneumonia, as tested against known lethal doses of pneumococci. They show that in many cases, at least, protective substances appear in the blood, and that in many cases these protective substances are active only against the race of organism concerned in the infection. They do not show that crisis and recovery are due alone to these substances. These substances have been demonstrated in the serum of immunized animals.

The local lesion in the lung is also probably concerned in recovery. Resolution almost certainly occurs through increase and associated breaking down of leukocytes, which finally sets free an amount of ferment sufficient to overbalance the antiferment of the serum, and to bring the fibrin into solution. It is conceivable that recovery may only occur when such a balance exists, and there is an outlet for the exudate.

It is not unlikely that all the factors, phagocytosis and increase of opsonin, neutralizing or antibacterial immune bodies, and leukocytic ferments, are concerned in recovery.

VACCINE THERAPY.—Rosenow and Hektoen have advocated treating pneumonia with partially autolyzed pneumococci. Rosenow had previously shown that when pneumococci are suspended in physiological salt solution, the substances on which their virulence and resistance to phagocytosis depend pass into solution. The soluble part at a certain stage was found very toxic, but had very little immunizing action, while the insoluble residue had marked antigenic properties, and protective action against experimental pneumococcus infection. Rosenow and Hektoen have reported a decrease in mortality in treating pneumonia with vaccines prepared in this way.

The results of vaccine therapy in general, have not been very encouraging. There is some evidence in favor of prophylactic vaccination in epidemics.

SERUM THERAPY.—Since the demonstration of protective substances in the serum of immunized animals, numerous contributions have been made to the subject. A definite lowering of the mortality from serum therapy has not been shown, but in general it seems that in many cases good results were shown in the course of the disease.

The most important advance in serum therapy was made by Neufeld and Händel in 1909. They found that the difficulty in obtaining a reaction to pneumonia serum was due to the fact that there are various strains of the pneumococcus which can be separ-

ated. A serum produced by one strain has no effect upon infections produced by other strains.

The subject has been further studied by Dochez and Gillespie, and they have grouped the strains or types into four classes. Two are fixed types with distinct serological reactions. The third type is the pneumococcus mucosus, for which no serum has yet been found. There is a fourth group, which does not have the same serological reactions as the first two fixed types, and includes numerous strains. It has also been shown in animals that there is a maximum degree of infection against which no amount of serum will protect.

Cole, at the Rockefeller Institute, believes that if he is able to determine the type of pneumococcus, results can be obtained by giving homologous antiserum intravenously. Following the work of Dochez, he has been able to produce an active immunity in animals for each one of the four groups, and an antiserum for the first and second groups. Cultures are made from blood, sputum, or lumbar puncture, the isolation of the pneumococcus from the sputum being accomplished by passage through the abdominal cavity of a mouse. The group to which the particular strain belongs is determined by agglutination reactions. In the first experiment on the therapeutic use of the serum, twenty cases were included. Two of these died shortly after entry into the hospital, and one was shown later to be caused by type 4. Of the remaining seventeen cases, fourteen were due to the first type of organism, and three to the second type. 2 cc. of antiserum were injected subcutaneously as a precaution to determine whether the patient was hypersensitive, and as soon as the type of organism was determined, 50 to 100 cubic centimeters diluted one-half with salt solution were injected intravenously. This was repeated at various intervals, depending upon the patient's condition. The solution was not given oftener than every twelve hours, and the doses varied from 190 to 460 cc. In four cases due to the first type of organism, all recovered except one. In three cases due to the second type, one patient died, but in this case the treatment was not thoroughly carried out. It was shown that the serum had marked bactericidal effect, and that with one treatment the blood of the patient was found to be sterile. Protective substances appeared shortly after the first injection. This work is very suggestive.

In order to use immune serum effectively in treatment, as in prevention, it is necessary to employ the serum specific for the group of organisms to which the special organism causing the infection belongs.

It is probable that the methods of application of such serums will be improved, and it is possible that the method may be combined with other measures directed toward other factors which are important

for the outcome. In any case, facts regarding the nature of the disease are being disclosed, and the outlook is encouraging. It is, however, in adults that the disease is so severe that specific treatment is sorely needed.

HYPOSTATIC PNEUMONIA

Hypostatic pneumonia is an extreme degree of passive congestion which occurs in the course of many long-continued diseases, such as typhoid fever. The dependent portions of the lungs become engorged with blood and the alveoli partially filled with accumulated alveolar cells, so that the condition resembles a consolidation. It occurs especially in patients whose vitality has been greatly lowered by a prolonged illness, and who are kept too long in one position without being turned.

The physical signs are those of slight dulness on percussion, generally at the base of the posterior lobes, diminished tactile fremitus, and feeble respiration and voice-sounds. Moist râles, generally bilateral, are heard over the areas of dulness, but fever, pain, and cough are absent.

The condition is recognized by the presence of the primary disease and by the gradual development of the physical signs without the characteristic features of pneumonia or pleurisy. It may, however, give no evidence of its presence during life, and may be discovered only at the autopsy.

TREATMENT.—The treatment is chiefly prophylactic during the course of the primary disease. The nurse should see that the child is not allowed to lie in one position for more than two hours. The condition calls for active stimulation.

GANGRENE AND ABSCESS OF THE LUNG

Gangrene and abscess of the lungs are represented essentially by the same clinical symptoms, and may occur in connection with lobar or bronchopneumonia. They are caused by the action of suppurative and putrefactive bacteria which invade the affected portions of the lung with the production of small or large abscesses.

Gangrene is diagnosticated chiefly by the presence of putrid, purulent sputum containing elastic fibres. It is to be distinguished from fetid bronchitis, which does not contain the elastic fibres of the lung-tissue.

The rupture of an empyema into a bronchus, with the resulting expectoration of purulent sputum, simulates the condition of abscess, but the diagnosis should be made by the presence of the physical signs of empyema. The treatment is that of the primary disease.

ATELECTASIS

Atelectasis is a collapsed and unaërated condition of the air vesicles. It may be congenital or acquired. Congenital atelectasis has been described under Diseases of the Newborn. Acquired atelectasis is a symptom of a number of diseases, and occurs especially in severe cases of bronchitis in which the smaller bronchi are involved, also in bronchopneumonia and in pertussis. Acquired atelectasis undetected during life is frequently found at the postmortem examination of infants and young children dying of almost any disease.

EMPHYSEMA

Emphysema is an over-distention of the alveoli and infundibula of the lungs. It is always a secondary process. Various descriptive terms have been used to denote differences in type of the disease.

Compensatory Emphysema consists in a dilatation of the alveoli in certain portions of the lung as a result of obliteration of the function of other parts by consolidation, adhesions, or pressure of deformed bones. This condition is likely to occur in connection with pneumonia, tuberculosis, chronic adhesive pleurisy, or rachitis.

Obstructive Emphysema represents the same pathological lesions, but the cause lies in some obstruction to expiration, as in stenosis of the larynx, asthma, and pertussis.

Interstitial Emphysema occurs rarely as a result of a rupture of the walls of the alveoli, by which the air works through the interstitial tissue of the lung.

SYMPTOMS.—Hyperresonance on percussion, feeble breathing, prolonged expiration, diminution in tactile fremitus and voice-sounds are the physical signs of emphysema. The normal area of cardiac dulness may be much diminished by the overlapping emphysematous lung; in the same way the upper border of the liver dulness may be considerably lowered. The other symptoms are those of the disease in which the emphysema occurs.

TREATMENT.—The treatment should be adapted to the underlying condition.

BRONCHIECTASIS

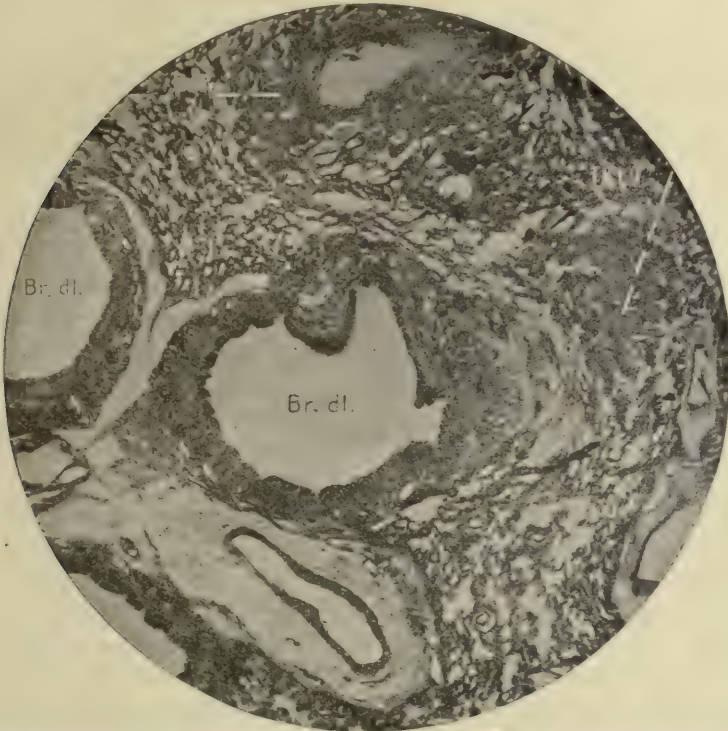
This is a condition of pathological dilatation of the bronchi.

ETIOLOGY.—Except for certain very rare cases of congenital origin, bronchiectasis is always a secondary condition, and follows various diseases associated with severe cough. It may develop as a result of whooping-cough, or after bronchopneumonia, the dilatation of the bronchi being due to the excessive intrathoracic pressure which accompanies the severe attacks of coughing. It is occasionally seen after measles. Pleurisy with fibrous tissue contraction, may

lead to bronchiectasis, through inspiratory traction on the bronchial walls. The condition is rare in the first three years of life.

PATHOLOGICAL ANATOMY.—The lesions are found most often in the lower lobes. There are numerous rounded or cylindrical dilatations of the bronchi, which are usually about the size of peas, but occasionally single much larger dilatations are found which may reach the size of a hen's egg. There is atrophy of the mucous membrane, loss of epithelium, and stagnation of the contents of the dilated bronchi.

FIG. 204



Chronic broncho-pneumonia. Br. dl., dilated bronchus; Th. L. T., thickened lung-tissue
Br. Pn., broncho-pneumonia

SYMPTOMS.—The typical manifestation of bronchiectasis is a prolonged attack of coughing. This occurs usually in the morning when the child gets up. Cough may be almost continuous for an hour. The attack ends with the abundant expectoration of a sputum which is often of foul odor. The child is then free from cough for a considerable time; there may be a second attack in the course of the day, or no further cough till the next morning.

On physical examination, the usual finding is a collection of coarse moist râles in some particular part or parts of the chest. An important

diagnostic point is that before the attack of coughing there can often be found an area of slight dulness or of tympanitic resonance, which disappears after the completion of the profuse expectoration. Signs of cavity are rare.

The course of the disease is extremely chronic. There may occasionally be slight rises of temperature, but other general symptoms are rare. Prolonged cases may lead to cardiac hypertrophy, disturbance of circulation, and eventually to clubbing of the finger tips.

DIAGNOSIS.—The conditions particularly to be considered in differential diagnosis are chronic bronchitis and chronic pulmonary tuberculosis with cavity formation. A certain amount of chronic bronchitis always accompanies bronchiectasis, and the latter condition is recognized by the peculiar characteristics of the cough and sputum. Tuberculosis is eliminated by the finding of a negative tuberculin reaction, and by the continued absence from the sputum of tubercle bacilli.

PROGNOSIS.—The prognosis is not very favorable. When once the condition of bronchiectasis has developed, there appears to be little tendency toward repair. Eventually, some complication such as pneumonia, empyema, or abscess of the lung is apt to develop.

TREATMENT.—The general treatment is that of chronic bronchitis.

ASTHMA

(Bronchial Asthma.)

Asthma is characterized by sudden paroxysms of severe dyspnea, accompanied by signs of bronchitis, and recurring at intervals of varying length. It is difficult to draw from the literature any conclusion as to the frequency of asthma in early life, because of the difference in the opinion of various writers as to what constitutes true bronchial asthma. Severe dyspnea, having a more or less paroxysmal character, is not uncommon as a manifestation of bronchitis in early life, particularly in infancy. Although the symptoms in such cases may closely resemble the paroxysms of true asthma seen in adults, nevertheless I believe that from an etiological point of view the condition is an entirely different one. The dyspnea is not due to a primary spasm of the bronchioles, but is only a symptomatic manifestation of bronchitis in early life, its paroxysmal character probably being due to the excitability of the nervous system, which so often modifies the symptoms of disease in childhood. The essential feature of true asthma is its *recurrence at intervals*, independently of any infection of the air passages. Under this restriction, only that form of paroxysmal dyspnea which resembles the disease as seen in adults, will be classified as asthma.

Asthma is certainly less common in childhood than in adult life. Nevertheless in a certain proportion of adult asthmatics the disease began at some time during childhood. True asthma is rare in infants. The disease is seen with increasing frequency after the fifth year.

The pathological process in asthma is chiefly a spasm of the unstripped muscular fibres in the walls of the bronchi. There is also a certain amount of exudation, causing swelling of the mucous membrane. The result of these factors is a constriction of the bronchial lumina.

ETIOLOGY. FORMER THEORIES.—Until recently, current views as to the etiology of asthma regarded the spasm as most probably a central neurosis of reflex origin. Under this view due prominence was given to the constitutional factor which must always be invoked to explain the occurrence of such a neurosis in certain individuals only. Undue prominence was given to the various possible sources of reflex irritation, which might act as precipitating causes for the attack. The disease was most generally regarded as due to the combination of a constitutional nervous excitability with reflex precipitating causes. The weak point in this explanation was the question why increased excitability of the central nervous system should lead to manifestations so peculiarly local as bronchial spasm.

THE CONSTITUTIONAL FACTOR.—There is no doubt of the importance of the constitutional factor in the etiology of asthma. Only such a factor can explain the occurrence of the disease in particular individuals. Many writers believe that the constitutional factor is the principal one in etiology, laying stress upon the association of the disease with eczema, and with the so-called "arthritic diathesis." So important is the constitutional factor, that, were it not for the peculiarly localized respiratory manifestations, asthma would be better classified among the diseases described in Division VI., on the conditions due to disturbances of metabolism or to constitutional anomalies. There is much difference of opinion, and no certain knowledge, as to the exact nature of the constitutional anomaly concerned in asthma. Some writers (Rachford), believe that asthma is closely associated etiologically with such conditions as migraine, recurrent vomiting, urticaria, diabetes, spasmophilia, and so forth. Rachford believes that the essential cause is a food intoxication. There can be no doubt that the constitutional anomaly, whatever its exact nature, is in many instances hereditary.

The presence of a constitutional factor in etiology throws no light on the particular pathogenesis of the disease. Why is bronchial spasm the essential disease manifestation? The most recent researches have suggested an answer to this question, which, if not absolutely proven for all cases of bronchial asthma, is at any rate highly probable.

ASTHMA AND ANAPHYLAXIS.—The most probable view as to the etiology of asthma regards the condition as a manifestation of *anaphylaxis*. For a full description of the phenomenon of anaphylaxis, the reader is referred to the literature of immune reactions. The essential feature is that the parenteral introduction into the body of a foreign protein leads to the development of a specific proteolytic ferment. The development of this substance is called "sensitization," and the ferment is stored in the body cells until activated by a second introduction of the same protein. The rapid splitting of protein which follows a second injection may lead to the liberation of poisonous constituents of the protein.

The evidence as to the association of asthma with anaphylaxis may be summarized as follows: *It is generally agreed that asthma is due to a stenosis of the bronchioles. It has been demonstrated that in animals dying from anaphylactic shock, the cause of death is a stenosis of the bronchioles.* Under this view asthma is a manifestation of anaphylactic shock in an individual who has become sensitized to a particular foreign protein substance. As anaphylaxis is a peripheral phenomenon, asthma is also peripheral, not a central neurosis.

There is considerable further evidence in support of this view of the etiology of asthma. Talbot has shown that many cases of asthma in children are due to egg-poisoning, the egg albumen being the sensitizing substance. Sensitization to egg albumen may be shown by a cutaneous test, performed by scarifying and inoculating the skin in the same way as for the von Pirquet tuberculin test. The phenomenon of horse asthma, in which the attacks develop when the subjects come into contact with horses, has long been recognized. The sensitization of these patients may be shown by a positive cutaneous reaction with horse serum. The association of asthma with the pollen of particular plants, with a specific cutaneous reaction, has been demonstrated. Research is demonstrating from time to time that other foreign substances are capable of producing sensitization in constitutionally susceptible individuals.

There are still many unsolved problems, which will be outlined under Problems and Research. Among them is the rôle played by various sources of reflex irritation as exciting causes of the attacks. There is much clinical evidence in favor of the etiologic importance of various conditions in the nose or pharynx, such as hypertrophic rhinitis, adenoids, hypertrophied tonsils, and elongated uvula. Such exciting causes as high winds, dust, cold or damp air, have appeared to play a part. Even if we accept the anaphylactic theory,—and I believe it should be accepted for many if not all cases of asthma—we cannot exclude a possible contributing part played by local irritation. Nevertheless I believe the rôle of reflex irritation is not based on

incontrovertible evidence, and that its importance has probably been overestimated.

The constitutional theory of etiology, is, however, in no way incompatible with the view that asthma is a phenomenon of anaphylaxis. On the contrary, it is a necessary conception in explaining all anaphylactic manifestations.

SYMPTOMS.—The symptoms of bronchial asthma are the same in the child as in the adult. A catarrhal condition of the respiratory tract, especially of the bronchi, may or may not precede the attack. The onset is usually sudden, and generally occurs at night. The child is seized with distressing dyspnea, mainly expiratory, the respiration being accompanied by a wheezing sound. The face is anxious, and if the attack continues for some time it becomes slightly cyanotic. The respirations are not especially increased in frequency. The pulse is rapid, and when the dyspnea is very intense, becomes weak. The temperature is not raised, and when the paroxysm is prolonged, it may become subnormal. The physical signs are mostly diffuse sibilant and sonorous râles, rhonchi, and muscular rumbles, which obscure or render inaudible the respiratory murmur. The attack may last for a number of hours, or even for days. The paroxysms vary in their severity, and, as a rule, are followed by considerable exhaustion. The frequency of the attacks varies; they may occur often or only at intervals of months.

There is a form of recurrent bronchitis, characterized by sibilant râles throughout the chest, which is often spoken of as recurrent sibilant bronchitis. Some writers regard this condition as due to the same etiological factors as cause asthma, while others regard it only as representing recurrent attacks of ordinary bronchitis, due to the same cause as is concerned in bronchitis, namely, infection of the air passages. This question is still unsettled.

DIAGNOSIS.—Attacks of true asthma are usually easily recognized. The paroxysmal character of the dyspnea, the prolonged wheezing expiration, and the tendency to recurrence, form a sufficiently characteristic clinical picture.

Positive confirmation of the diagnosis may be obtained by examining the blood and the sputum. The blood picture in asthma is characteristic, the essential feature being a marked increase in the number of eosinophiles. The percentage of eosinophiles is always increased, averages about 10 per cent, and may be as high as 20 or 25 per cent. The examination of the sputum is important mainly in older children. It usually contains numerous eosinophiles. The Charcot-Leyden crystals and Curschmann's spirals which are so constant in the sputum of adult asthmatics, are usually only found in the sputum of older children.

The various forms of paroxysmal dyspnea seen in children, sometimes designated as "false asthma," are excluded mainly by the examination of the blood. This is the only way in which we can exclude true asthma when paroxysmal dyspnea occurs as a manifestation of bronchitis or bronchopneumonia in infants. Paroxysmal dyspnea is not so often a symptom of cardiac or renal disease in children as in adults, and "cardiac asthma" and "renal asthma," rarely have to be considered in differential diagnosis. The spasm of the larynx seen in catarrhal laryngitis (common croup), produces paroxysmal dyspnea, but the condition is easily recognized by the inspiratory character of the dyspnea, by the inspiratory stridor, and by the absence of râles in the lungs. Thymic asthma is a condition associated with paroxysmal dyspnea, but in it the prolonged wheezing expiration is absent, the breathing is not so labored, and the characteristic blood picture is absent.

PROGNOSIS.—The prognosis of asthma is generally stated to be best in the so-called "catarrhal" asthma of infants, and in older children when the disease is due to some removable local source of reflex irritation. In many of these cases, in which a favorable course developed as the infant grew older, or followed local treatment, the evidence was not clear that the disease was true asthma. I cannot deny that a favorable effect, even in true asthma, has followed local treatment of the nose and throat, but in my experience such cases have been comparatively uncommon. In the majority of my cases of true asthma, the disease has resisted such treatment.

I believe that the prognosis is mainly dependent upon how marked is the constitutional factor in an individual case, and this is a point which we cannot determine. It is further dependent upon the nature of the foreign substance which excites the attacks, and the ease with which it can be discovered. There is much promise in specific treatment by immunization of those cases which can be shown to be sensitive to the pollen of a particular plant, or to egg albumen or some other particular food substance.

TREATMENT.—The treatment of asthma may be divided into the measures used for the symptomatic relief of the attack, and those used in the general treatment of the disease.

TREATMENT OF THE ATTACK.—Inhalation of the fumes of nitre paper, or stramonium leaves is the measure which should ordinarily be used in the acute attack. Most of the proprietary "asthma cures" contain these ingredients. The child's room may be filled with the fumes, and if this is not effective, the fumes should be introduced into a tent made as described for croup. If the attack is very severe, or if the inhalation of nitre or stramonium fumes fails to give relief, an intramuscular injection of epinephrin (adrenalin

chloride 1 to 1000 solution) should be given. The dose is $\mathfrak{m}$ v to $\mathfrak{m}$ viii according to age for a child over three years. Epinephrin is undoubtedly the most powerful available means for relieving the asthmatic paroxysm, although the effect is transient. It has been shown that this drug extends the lumina of contracted bronchioles.

With these measures available, it should never be necessary to use morphin in the asthma of children. Codein is sometimes useful in resistant attacks, as it may give a more lasting relief than epinephrin. Many writers believe that the nocturnal attacks can be aborted or lessened in severity by the giving at bedtime of one of the nervous sedatives, such as antipyrin or bromide. I have never been able to convince myself that the apparent improvement which only sometimes follows the institution of bedtime doses of antipyrin or bromide was certainly a phenomenon of cause and effect, but there is no objection to trying this treatment, doses being proportioned to the age of the child.

No matter how severe the dyspnea, the cold air treatment is absolutely contraindicated in an attack of asthma. Warm moist air at a temperature of 70° F. is best, but the child's sleeping room should be well ventilated.

In order to avoid all possible sources of reflex irritation, the physician should make sure that the bowels are thoroughly open, and if any doubt exists on this point, an enema should be given at the beginning of the attack, and the bowels should be kept open during the subsequent period.

GENERAL TREATMENT OF THE DISEASE.—The most important indication in the general treatment of asthma is to try to determine if the attacks are associated with any particular foreign protein. Cutaneous inoculation tests should be made with egg albumen, and with the various other articles of food which enter into the child's diet. There are now available for purposes of diagnostic vaccination, preparations made from the pollen of various plants, and if the asthma occurs only in the spring, summer or autumn, cutaneous tests for sensitization toward these pollens should be made.

If any food substance is incriminated by these tests, it should be excluded from the child's diet. In the treatment of asthma due to egg poisoning, Schloss and Talbot have attained success by a method of gradual immunization through the ingestion of very small quantities of the foreign protein. This method may be tried with other incriminated food substances. A similar method of gradual immunization against pollen has been attended by success in the asthma and hay fever of adults, and this form of treatment could be tried in suitable cases in children. This method of treatment, however, while very promising, is still in an experimental stage, and should only be undertaken by one trained in its use.

Children sensitive to pollen should spend the time during which the particular plant is in bloom in some locality where it is not found. Children susceptible to the odor of horses or other animals should be kept from contact with them.

In a certain number of cases, the specific cause of the asthmatic attacks will not be disclosed by any of the above procedures. The association of asthma with bronchitis, suggests that the sensitizing protein may be of bacterial origin. The patient should receive the same treatment as is indicated for chronic bronchitis, the essential feature of which is *complete change of climate* whenever possible.

While I believe that the rôle of reflex irritation has been exaggerated in asthma, there is evidence that it may constitute a precipitating cause. The nose and rhinopharynx should be carefully examined in every case of asthma, and any pathological condition should be properly treated. I have, however, seen very few cases of asthma in children relieved by such measures as the removal of adenoids or hypertrophied tonsils. Exposure to such possible precipitating causes as cold damp wind, dust, and so forth, should also be guarded against.

The diet of the asthmatic child should be carefully scrutinized, and any faults should be remedied. While I believe that too much emphasis has been placed upon the specific influence of diet in constitutional diseases, the possible rôle of an improper diet as a contributing cause cannot be neglected. Only, there is no convincing proof in asthma of the importance of any particular dietary regimen, and the diet should be arranged in accordance with the general principles which govern the selection of the food for a child of that age. It is well, however, to try the complete exclusion of *sweets, eggs, and cream*.

For medicinal treatment in the interval between attacks, the preparation usually recommended is iodide of potassium, or syrup of hydriodic acid. While these iodides can do no harm, I have never been convinced of any real benefit from their use in asthma.

PROBLEMS AND RESEARCH.—The central problem in asthma is whether all cases represent a manifestation of anaphylaxis, or whether there are any cases which represent a central neurosis. The tendency of recent experimental research is to relegate more and more cases to the anaphylactic group. If it be eventually shown that true asthma is always an anaphylactic phenomenon, our theories of the importance of reflex irritation as a precipitating cause will be open to serious question.

Experimental work has mainly been confined to the demonstration in asthmatics of a positive cutaneous reaction with various food substances, animal sera, and plant pollens. There is an extremely interesting experiment by Manirloff, bearing on the anaphylactic

nature of asthma. He injected animals with the serum of an asthmatic, thus supplying the constitutional factor, and then injected a solution made from the Charcot-Leyden crystals of the asthmatic sputum. Severe anaphylaxis developed in the animals thus treated, while there was none in the controls. The investigator concludes that the crystals, due to the products of protein decomposition, are the cause of the attacks.

The relation of asthma to bronchitis and other infections of the upper respiratory tract is interesting in connection with the possible cases of asthma which cannot be proven to be due to food protein or plant pollen. The question arises whether in some cases of asthma the sensitization may not be due to protein substances derived from the bodies of bacteria. Koessler and Moody found various anaerobic organisms in the sputum of asthmatics, and believe that sensitization is produced by the parenteral entrance of fragments of foreign protein derived from such organisms. Under this theory the bronchitis is primary, the patient becomes sensitized to the infecting agent associated with his cold or bronchitis, and the continued presence of the same organism in the bronchi accounts for the violent action on the muscles of the bronchial walls. This theory is very suggestive.

III. PLEURISY

This is the only important disease of the pleura which occurs in early life. From the point of view of pathological anatomy, the same forms of inflammation of the pleura occur in childhood as in adult life, namely, fibrinous "dry" pleurisy, pleurisy with serous effusion, and pleurisy with purulent effusion. The most important difference between childhood and adult life is the very much greater frequency with which purulent pleurisy is encountered in the former.

Pleurisy is always caused by bacterial infection. In the great majority of cases the infection extends to the pleura from the lung. Occasionally the disease may result from an extension of inflammation from one of the neighboring organs, and pleurisy is an occasional complication of peritonitis, perihepatitis, perityphlitis, perinephritis, and pericarditis. Pleurisy is an occasional manifestation of rheumatic fever, the inflammation of the pleura probably representing an extension from the pericardium. It has been a much discussed question whether pleurisy is always a secondary infection, or whether primary pleurisy may occur. As very slight infectious processes in the lung may extend to the pleura, it is probable that the cases of pleurisy which have been considered to be primary really represented a secondary infection in which the primary inflammatory process was overlooked.

The following forms of pleurisy will be considered:

1. Purulent pleurisy (Empyema).
2. Serous pleurisy.
3. Fibrinous pleurisy.
4. Chronic adhesive pleurisy.

EMPHYEMA

This form of pleurisy is considered first, because it is by far the commonest form encountered in early life.

ETIOLOGY.—In the great majority of cases, empyema is a complication of some form of pneumonia, the infecting organism reaching the pleura by direct extension from the lungs. Empyema, while occurring in all forms of pneumonia, is commoner in lobar pneumonia than in bronchopneumonia, and most often complicates the type described as pleuropneumonia.

Among the rarer sources of infection in empyema may be numbered pyemia, infectious disease of the newborn, suppurative arthritis, osteomyelitis, appendicitis, purulent peritonitis, purulent pericarditis,

traumatism, necrosis of a rib, and the rupture into the pleura of abscesses situated in the mediastinum, thoracic wall, or peritoneal cavity.

The *pneumococcus* is the organism most frequently found in the exudate of empyema in early life. In my experience the pneumococcus is present either alone or associated with other organisms in about 80 per cent of cases of empyema in infancy. Holt found the pneumococcus present alone in 64 per cent of 180 cases, and in his series 12.8 per cent were mixed infections in which the pneumococcus was present in two-thirds, giving a total of 72 per cent. These figures are in marked contrast to those for empyema in adults, in which the pneumococcus is only found in about 25 per cent. There can be no doubt that the pleura of the young child is especially predisposed toward pneumococcus infection. The *streptococcus* and *staphylococcus* are sometimes found alone, sometimes in mixed infections. The *tubercle bacillus* is very rarely the cause of empyema in infancy and early childhood, but tuberculous empyema is sometimes seen in cases occurring after the seventh year. The *bacillus of influenza* is very rare as the sole cause, but is sometimes seen in the mixed infections.

Empyema is particularly a disease of infancy and early childhood. It is comparatively uncommon, but not rare in the first six months, common in the second six months, and still more frequently encountered in the second year. From this time it gradually diminishes in frequency from year to year. On account of the usual association of empyema with pneumonia, it follows that the disease is more frequent in the winter and spring, and somewhat more frequent in males than in females.

PATHOLOGICAL ANATOMY.—The inflammatory process begins with an exudation of fibrin upon the surface of the pleura, accompanied by an excessive migration of leukocytes and a rapid accumulation of pus. The exudation may occasionally be sero-fibrinous at first and subsequently become purulent. In cases of streptococcus and staphylococcus infections, the inflammation may be purulent from the beginning, but the pus is not so thick and contains less fibrin than in pneumococcus infections. The pus may be encapsulated, and this condition of localized empyema is not uncommon in infants.

The pus is usually thick, creamy, and without odor. The quantity of fluid ordinarily is from four ounces to a pint, but in long-standing, neglected cases may be much larger. In children the fluid, even when small or moderate in amount, does not, as in the adult, tend to collect at the bottom of the pleural cavity, floating the lung upward, but tends to spread through the whole pleural space in a layer

which varies in thickness with the quantity of fluid. Only the apex of the pleural cavity is free when the quantity of fluid is small, and when it is moderate, all parts of the lung are surrounded. When the quantity of fluid is large, the lung is not pushed upward, but is compressed from all directions toward the hilus. These peculiarities in the distribution of the fluid in childhood are highly important in explaining the differences in the physical signs of pleuritic effusion in early life from those in adults.

When cases of empyema are given proper treatment, the pressure is removed comparatively early in the course of the disease, and although fibrinous adhesions may be present, they are not sufficiently firm to resist the effect of coughing and to prevent expansion of the lung. In such cases absorption of the exudate may be complete, or at most there may be some organization by fibrous tissue formation which leads only to a thickening of the pleura, but does not interfere with function. When the disease has been long continued, there is pronounced fibrous tissue formation, which causes not only marked thickening of the pleura but also fibrous adhesions which may be so dense and firm, that expansion of the lung is prevented or is incomplete. Expansion may be further interfered with by fibrous organization in an unresolved pneumonia. In these cases, the empyema is followed by recession of the chest wall.

When empyema receives no treatment, absorption of the pus is possible, but very unusual. If the child does not die from the exhaustion caused by so prolonged a septic process, the pus usually eventually seeks an external outlet. Perforation of the lung may occur, the pus being evacuated through a bronchus, or the empyema may rupture externally, the so-called "empyema necessitatis." The usual point of external rupture is near the nipple. The pus may burrow into adjoining anatomical structures. The most common of these complications in children is pericarditis, although peritonitis is seen at times.

SYMPTOMS.—In the majority of cases of empyema, in which the disease develops as a complication of pneumonia, the time of onset of the pleuritic inflammation cannot be definitely established. This is especially true in infants, in whom the formation of pus in the pleural cavity often begins during the course of the primary disease, and the symptoms of the empyema are indistinguishable from those of the pneumonia. We can only suspect empyema in such cases from a continuance of the fever and other symptoms beyond the time when recovery from pneumonia was expected, or from some notable change in the signs found on physical examination. In other cases, the empyema may develop after a period during which the temperature has been normal or nearly normal. The

beginning of empyema in these cases is signalized by a rise of temperature which may be sudden, but is usually gradual, and by an increase in the signs of thoracic disease. When empyema is apparently primary, or complicates scarlet fever or some other acute infectious disease, the symptoms are fever, cough, rapid breathing, and pain which is often referred to the abdomen, and which in infants is manifested by whimpering, or an expiratory moan. It is probable that in these cases the primary disease is a pneumonia, of too slight an extent to reveal itself to physical examination. The signs of fluid in the chest may not reveal themselves for three or four days. In the tuberculous empyema sometimes seen in older children the onset is very insidious, with slight or moderate fever, and gradually increasing dyspnea and cachexia. Marked leukocytosis, 20,000 to 40,000, is always present, even in the earliest stage of empyema.

When the disease has become established, the symptoms are characteristic and fairly uniform. The temperature is very irregular, ranging usually from 101° F. to 103° F. or 104° F. A regular "septic" or "hectic" temperature with sweating is extremely uncommon in early life. The respiration is always accelerated, ranging usually from forty to eighty per minute. The breathing is ordinarily not difficult or labored, but in some cases dyspnea may be marked. The pulse is rapid, regular, and of fairly good quality. Cough is almost invariably present. Loss of flesh, anemia and prostration gradually become more and more pronounced.

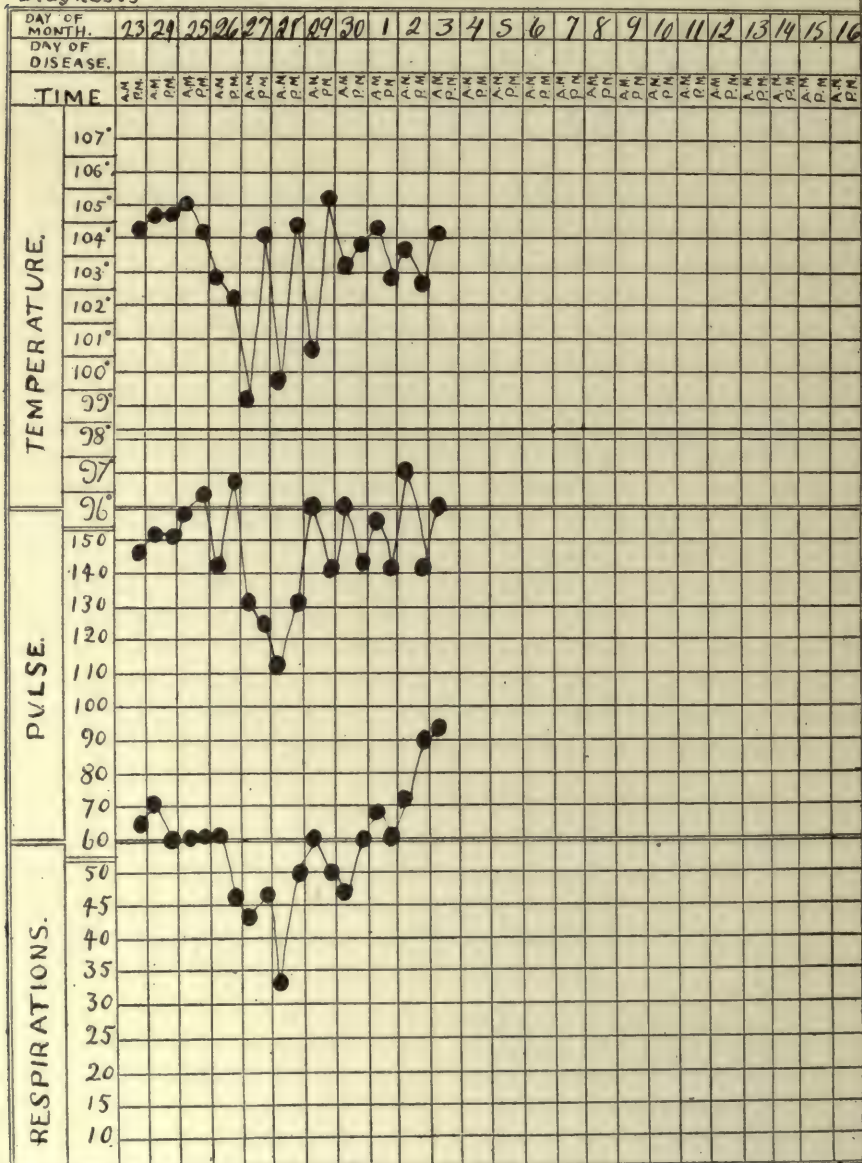
These symptoms usually persist more or less unchanged for several weeks. In some cases emaciation and prostration become so severe that the patient dies of exhaustion, this occurring most often in feeble infants. In other cases, a subacute stage may follow, which may last for many months. There is an apparent improvement, there being little or no fever, and the child regains strength and color. Nevertheless the cough and rapid breathing persist, and there is no change in the signs found on physical examination of the chest. In very chronic cases the general symptoms may resemble tuberculosis. Finally there may be albuminuria, edema, and clubbing of the finger tips.

PHYSICAL EXAMINATION. INSPECTION.—There is diminished respiratory movement of the affected side. If the quantity of fluid is considerable, the circumference of the affected side of the thorax is greater than that of the sound side. In some cases there is obliteration or bulging of the intercostal spaces. The apex beat of the heart is displaced in the majority of cases, the displacement varying with the amount of fluid. If the fluid is in the left side of the chest, the displacement of the apex beat toward the right is usually notable even with small quantities of fluid. If the right pleural cavity is

CHART 24

Mr. Abraham Goldman

Diagnosis



F. H. Thomas Co., 727 Boylston St., Boston.

Empyema complicating lobar pneumonia



FIG. 205—Empyema. Area of dulness with a small amount of exudate from in front.



FIG. 206—Empyema. Area of dulness with a small amount of exudate from behind.

affected, the displacement of the apex beat of the heart toward the left is less marked, and is not present with small quantities of fluid.

PERCUSSION.—The signs found on percussion are the most important in the diagnosis of pleuritic effusion in children. Provided that the proper method of light percussion be used, there is *flatness* rather than marked dulness over the area occupied by the fluid. Care must be taken not to percuss too heavily otherwise the thin layer found in the effusions of childhood may permit some resonance to come through giving a false impression of dulness rather than of flatness. A marked sense of resistance on percussion is always present with fluid, and is a valuable aid in recognizing flatness. The flatness and sense of resistance are often best elicited by slapping the chest.

The outline of the flatness is important in children. Even with a small amount of fluid, the flatness occupies a larger area of the chest wall than with a proportionate amount of fluid in the adult. The line of flatness always extends across the front of the chest. Cases in which the flatness occupies only the base behind are not seen in early life, if the fluid be free and not encapsulated. Only a small amount of fluid is required in order that the line of flatness shall rise high in the axilla, and continue across the front of the chest above the level of liver dulness. In typical cases with a small amount of fluid, there is flatness behind, below the midscapular region, or below the spine of the scapula, the line of flatness being high in the axilla, if not including the whole axilla, and being at least as high as the fourth rib in front. Above the area of flatness the percussion note is usually either slightly dull, or tympanitic. With moderate effusions there is flatness over the entire affected side of the chest except for a tympanitic area below the clavicle. With large effusions the flatness extends over the entire side of the chest.

The above description of the outline applies only to those effusions in which the fluid is free in the pleural cavity. With encapsulated fluid, the percussion note is flat, but the outline is in no way characteristic. Shifting of the outline with change of position has been described as often present with pleuritic effusions. Such shifting, in my experience, is almost never found in the effusions of early life.

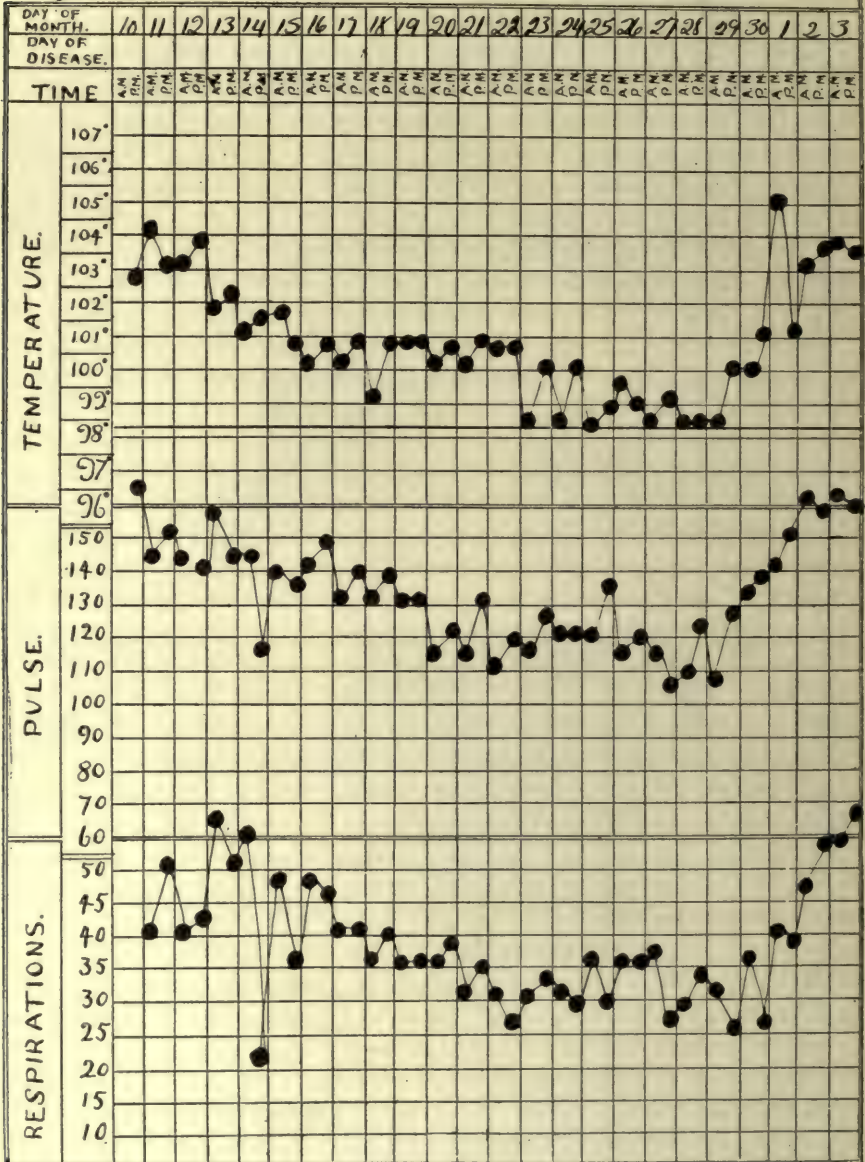
The percussion of the outlines of cardiac dulness is fully as important as that of the outlines of pulmonary flatness. In all free effusions in the left pleural cavity, the cardiac dulness is displaced toward the right, and it does not require a very large effusion to displace the relative cardiac dulness as far as the right nipple. In free effusions in the right pleural cavity, displacement of the heart is less marked and may not be noted with small effusions. With moderate effusions, the cardiac dulness on the left usually extends, beyond the nipple, and with large effusions, displacement is pronounced. In

CHART 25

Mr. Stella Muise

Sept

Diagnosis



F. H. Thomas Co., 727 Boylston St., Boston.

Empyema following bronchopneumonia

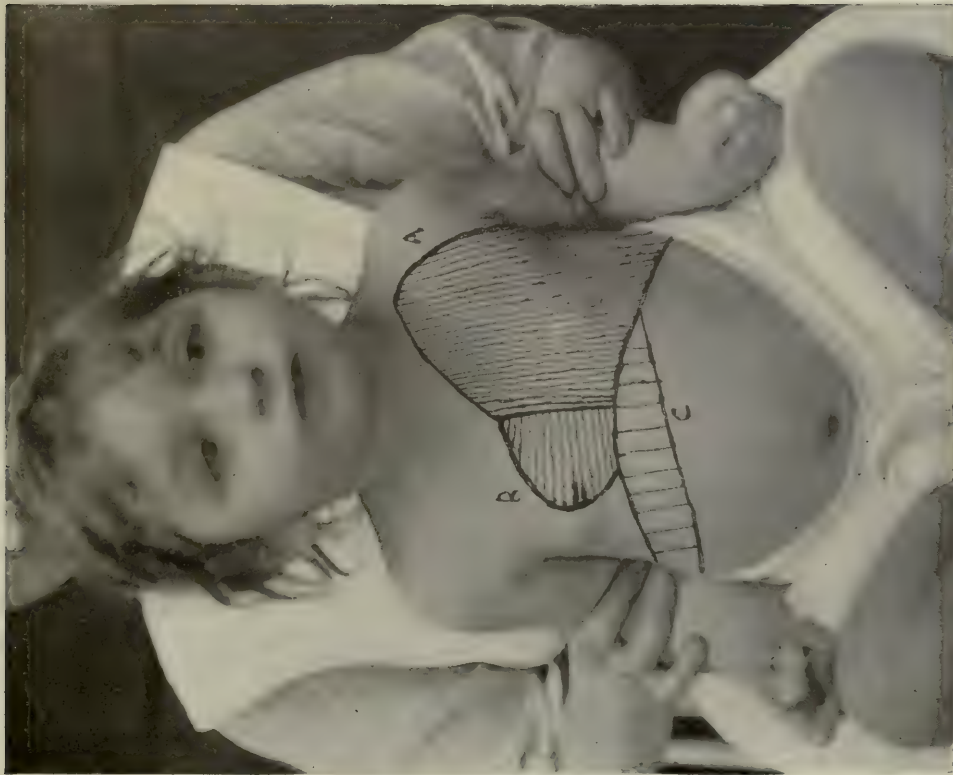


FIG. 207—Empyema. Area of dulness with moderate or large effusion from in front.
 A. Pulmonary dulness B. Cardiac dulness C. Hepatic dulness



FIG. 208—Empyema. Area of dulness with moderate or large effusion from behind.



FIG. 209—Empyema. Outlines of dulness with small effusion.
A. Pulmonary dulness B. Cardiac dulness C. Hepatic dulness.

general displacement of the heart in pleuritic effusion takes place much more readily in children than in adults.

Grocco's sign is found in most cases. This is a triangular area of dulness with its base toward the spine, situated at the base of the side opposite to the effusion.

AUSCULTATION.—The signs found on auscultation are much less useful in the diagnosis of pleural effusion in children than they are in adults. The respiratory murmur and voice sounds are usually, but not invariably, diminished in intensity, but this is by no means pathognomonic of fluid. Absence of breathing, and voice sounds points toward fluid, but is very exceptional. Bronchial breathing and bronchophony are very commonly heard over effusions in early life, and diminution in their intensity, while usually present in fluid, is also found over consolidation. Friction sounds are ordinarily not heard, but may be found above the level of the flatness. Râles are usually not heard, but moist râles may be present.

PALPATION.—The tactile fremitus is often diminished or absent but in children this sign is less commonly present, and less characteristic of fluid as contrasted with consolidation, than in adults.

DIAGNOSIS.—The most important point is the differential diagnosis between pleuritic effusion and pulmonary consolidation. Consolidation likely to be mistaken for effusion is found most often in lobar pneumonia, and tuberculous bronchopneumonia. Mistakes in diagnosis usually arise from the placing of too much dependence upon the auscultatory and tactile signs. In both effusion and consolidation, the respiratory murmur and voice sounds are usually diminished in intensity, and bronchial in character, and the tactile fremitus may or may not be diminished. Numerous râles point toward consolidation, but do not exclude fluid.

The essential diagnostic signs of free fluid as opposed to consolidation are the following: (1) The character of the dulness; (2) the outline of the dulness; (3) the displacement of the heart.

Flatness is not often present over lobar pneumonia, except in certain pronounced cases of the pleuro-pneumonia type. It is not often present over unresolved pneumonia unless there is very marked fibrous thickening of the pleura. It is sometimes present over a very extensive tuberculous bronchopneumonia, when the pleura is greatly thickened. The presence of flatness, while not a certain sign of fluid, is sufficient to warrant exploratory puncture.

The outline of the dulness in lobar pneumonia, both in the acute and unresolved stages, usually corresponds to the outline of a particular pulmonary lobe. When a lower lobe is involved, the dulness does not extend to the top of the axilla, nor does it occupy the front of the chest. When both lobes on the same side are involved in

pneumonia, the dulness may occupy the entire chest, and simulate the condition found in effusion. The same signs may be found in a massive tuberculous bronchopneumonia. Flatness over the whole side of the chest, however is always sufficiently suspicious of effusion to warrant exploratory puncture, and the same is true of flatness over both the back and front.

Displacement of the heart, when present is practically diagnostic of effusion. It is sometimes seen in long standing cases of tuberculosis or chronic interstitial pneumonia in which the heart is pulled over by fibrous tissue contraction, or after a foregoing empyema in which the heart is held displaced by adhesions. These conditions are rare, and do not usually give the other physical signs of effusion. Absence of cardiac displacement does not exclude a right-sided effusion. I should hesitate, however, to diagnose a left-sided effusion without displacement of the heart.

The above signs will usually enable the physician to make an accurate differentiation between free fluid and consolidation. A roentgenogram of the chest is often of great assistance in differentiating between fluid and consolidation, and is especially valuable as a diagnostic procedure when the physical signs are doubtful or conflicting. The essential features of the roentgenogram in pleuritic effusion, are the uniformity of the area of diminished permeability, and the fact that with free fluid the area is not confined to a single lobe, but either involves the whole side of the chest, or rises to a definite level. Displacement of the heart which cannot clearly be made out by inspection and percussion, will often show in the plate.

Whenever the signs are compatible with fluid exploratory puncture of the pleural cavity should always be performed. Only in this way can the diagnosis be positively confirmed. The diagnosis of encapsulated fluid from the physical signs is much more difficult because the outline of the dulness is not characteristic, and displacement of the heart is often absent. The diagnosis can only be made by means of exploratory puncture. This should be done whenever there is a persistent area of flatness, or of marked dulness associated with diminished breathing and an absence of râles.

Whenever exploratory puncture is undertaken, the physician should not rest content with the negative result of a single puncture, but several punctures in different parts of the flat area should be made, until the presence or absence of fluid is definitely determined. Any fluid obtained by exploratory puncture should be examined bacteriologically, as the type of organism concerned in empyema is of considerable prognostic significance.

I have occasionally seen a large pericardial effusion mistaken for a left-sided pleuritic effusion. The differential diagnosis depends

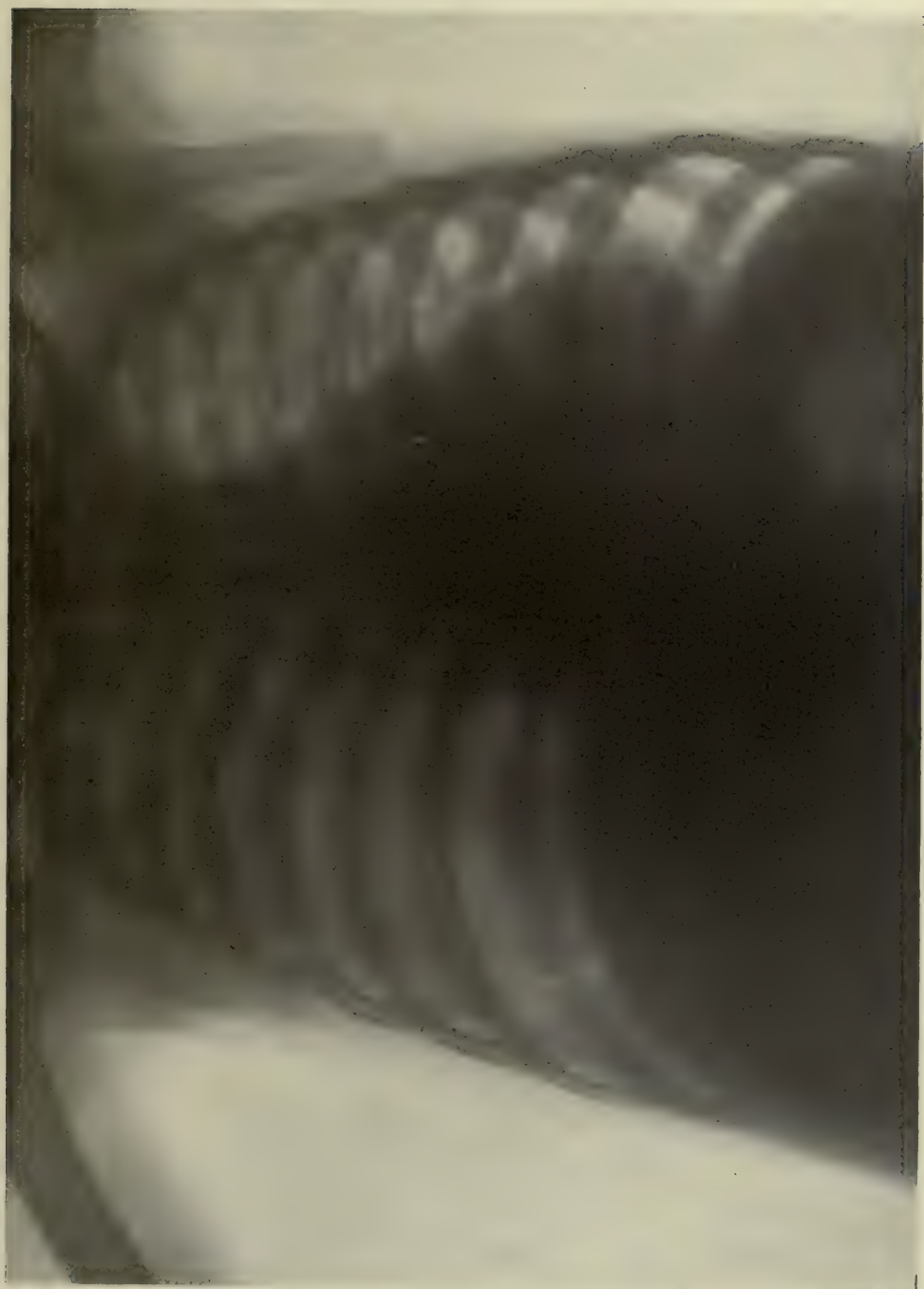


FIG. 210—Empyema with small effusion.

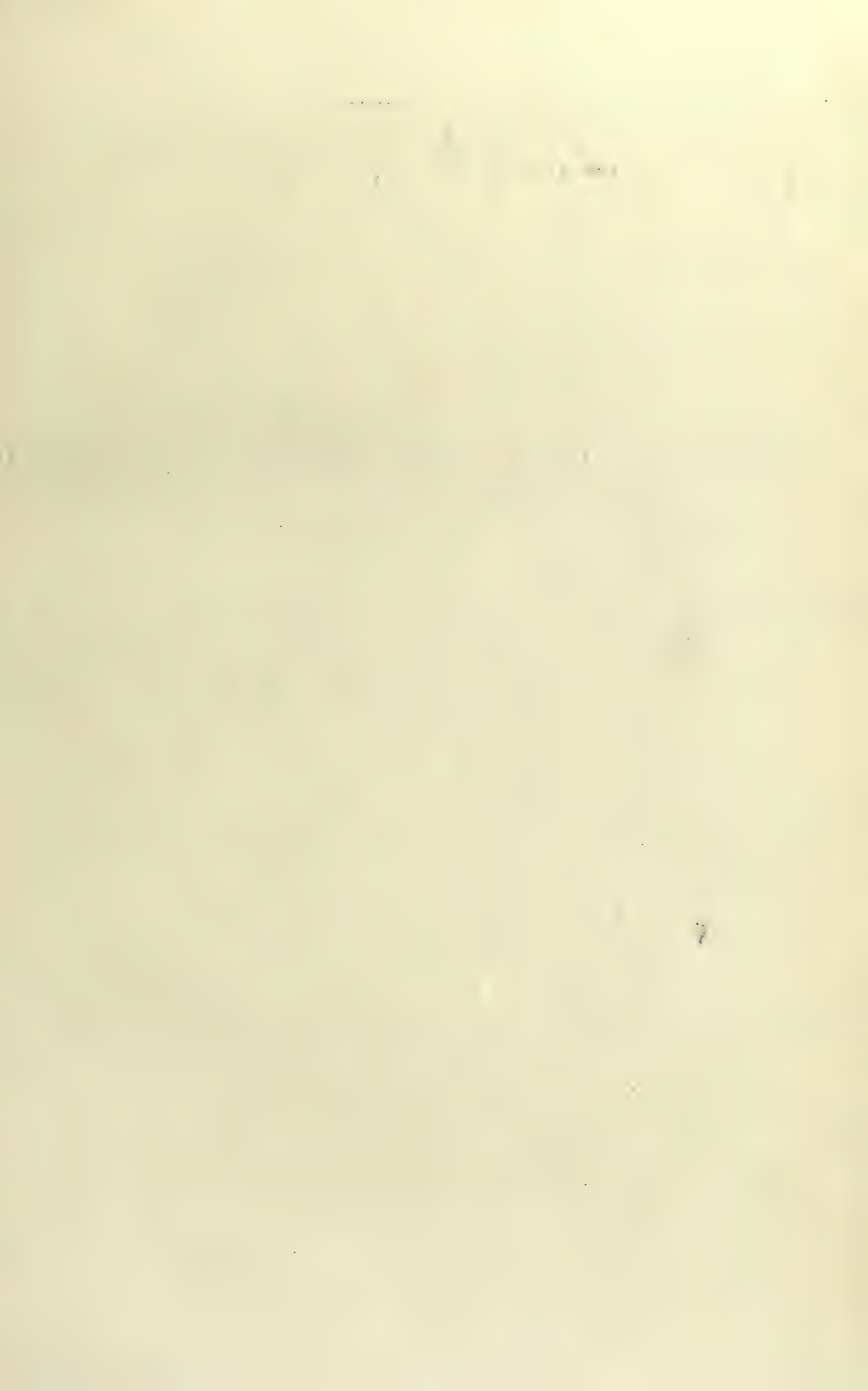




FIG. 211—Old empyema and unresolved pneumonia

mainly on the fact that in pericardial effusion the cardiac impulse is either obliterated, or is not displaced toward the right. The feeble character of the heart sounds is a significant feature with a large pericardial effusion. The differentiation can easily be made by a roentgenogram of the chest.

A large abscess of the lung can not be definitely distinguished from encapsulated empyema, either by physical examination, by exploratory puncture, or by roentgenogram. The diagnosis can only be made by operation or autopsy. Such abscesses are very rare in childhood.

The differential diagnosis between empyema and serous pleurisy cannot be made by physical examination, as the signs of fluid are the same in both conditions. In the majority of cases in infancy and early childhood, the fluid is purulent. A marked leukocytosis points toward empyema. In all cases with signs of fluid, exploratory puncture is indicated, and the diagnosis between serous and purulent pleurisy depends upon the result of this procedure.

PROGNOSIS.—The outcome in empyema depends upon the age of the patient, the duration of the symptoms, the type of organism causing the disease, the presence or absence of serious complications, and the treatment. The age of the patient is a very important factor. In general, even with early diagnosis, good general condition and proper treatment, infants with empyema tend to do badly, and the mortality of the disease is high—certainly higher than 50 per cent. The disease is particularly fatal in the first year of life. The explanation of the high mortality in infancy is not wholly clear, and cannot adequately be based on a lessened resistance to infection in general. While I cannot give positive statistical evidence in support of my observations, I have noted that fibrous adhesions preventing the lung from expanding are a much more common finding in autopsies of cases of empyema in infants than in older children. The cause of fatal ending in older children appears to be usually either that the case is due to a mixed or streptococcus infection, or else that proper treatment was postponed until the child was in too poor a general condition. In infants a fatal ending is common even in early cases with a pure pneumococcus infection. I believe it to be closely connected with a tendency to the formation of fibrous adhesions, which is probably due to the fact that the power of expanding the lung by coughing before such adhesions have formed is less in infancy than in later childhood. The unexpanded lung lessens the effectiveness of drainage, and the result is accumulation of pus, rise of temperature, and finally death from exhaustion.

The general condition at the time of operation has a very important bearing on the prognosis. A bad general condition due to other

causes may be present in cases treated early in the disease, and feeble babies usually die. A poor general condition may also be produced by a long duration of the disease before operation is performed.

The type of organism causing the suppuration in the pleural cavity is very important in connection with the prognosis. The outlook is most favorable in pure pneumococcus infections, and these are seen most frequently in the empyemas complicating lobar pneumonia. Staphylococcus infections are also comparatively favorable, although they are seen most often in infants, in whom the prognosis is bad for other reasons. Streptococcus and mixed infections give a very grave outlook. Tuberculosis is a rare cause in childhood, especially in the period before the seventh year, and is of grave but not necessarily fatal prognosis unless a mixed infection occurs.

Serious complications are uncommon in empyema. General pyemia and gangrene of the lung, which are important causes of a fatal ending in adults, are rare in childhood. Spontaneous rupture of an empyema into a bronchus or externally is seen in neglected cases, but does not in itself affect the prognosis either way. Pyopneumothorax is rare in early life.

The treatment is important in connection with the prognosis. Spontaneous recovery through absorption can occur, but is extremely rare. The mortality of empyema, while high in infants, was much higher both in infants and older children before the general adoption of surgical treatment.

In general, in a child over three years of age, with a good general condition, a pure pneumococcus infection, and early surgical treatment, recovery should occur. With cases of this type recovery is usually complete. Retraction of the chest and lateral curvature of the spine are only seen in neglected cases.

On the other hand, in a child under three years, the prognosis is always serious. If in addition there is a streptococcus or mixed infection, or a poor general condition, the outlook is very grave.

TREATMENT.—The treatment of empyema is surgical. There is some difference of opinion as to the preferable operation, the choice lying between simple incision and drainage, and incision with partial rib resection. The former operation has the advantages of requiring less time, no general anesthetic, and of being a less severe procedure. Furthermore there is evidence that with a small opening in the chest wall, expansion of the lung takes place more easily than when the opening is large. For these reasons, simple incision with drainage is the operation in infants preferred by most surgeons, although some authorities regard incision with rib resection as most satisfactory at all ages. The disadvantages of simple incision are that the small



FIG. 212—Empyema after operation. The Roentgenogram shows pneumothorax with marked displacement of the heart.

opening may not permit adequate drainage, either because of large masses of fibrin in the exudate, or because the drainage tube may become pinched between the ribs. These disadvantages are avoided by resection of about an inch of rib, and this operation is usually preferred in children over three years of age.

In general, the choice of operative procedure must depend upon the preference of the individual operator. There are various modifications of technic, such as Bulau's method of siphon drainage, which are matters of surgical technic, and will not be described in detail. Washing out the pleural cavity is not to be recommended, unless the pus be foul.

Some cases of empyema have been cured by simple aspiration. This method of treatment is not to be recommended, as the statistical evidence shows it to be less effective than incision and drainage, the reason being that the fibrinous masses and all the pus cannot be removed. Aspiration should only be employed as a means of temporary relief while the physician is waiting for surgical interference, and then only when there is an accumulation of fluid sufficiently large to produce serious symptoms. It should also be used in the treatment of one side in cases of double empyema, as an opening into both pleural cavities at once cannot be made with safety.

Some authorities advocate the delaying of operative interference until the most acute stage shall have subsided, this usually not occurring until two or three weeks after the invasion of the pleura. I believe that such delay is very inadvisable, and that *in empyema the operation should be performed as soon as the diagnosis is made*, unless the general condition of the patient is very bad. Even with a bad general condition, I do not believe there should be a longer delay than that required for the available measures of stimulation, not more than forty-eight hours. The reason that delay is inadvisable even in the acute stage, is that the chief cause of an unfavorable outcome after operation for empyema is the formation of adhesions preventing expansion of the lung, and each day of delay favors the formation of these adhesions.

After operation for empyema, the usual duration of discharge from the drainage tube is from three to six weeks. When discharge has ceased, the temperature remaining down, the tube is removed and the wound allowed to heal. The mistake is sometimes made of allowing the tube to remain in too long, which delays the closing of the sinus. If after operation for empyema the temperature remains elevated, or rises again after coming down, the usual cause is defective drainage. This is most often due to blocking of the tube. Continued temperature or a fresh rise of temperature may be due to some other cause, such as the underlying pneumonia, a fresh pneumonia, an abscess of the lung, pericarditis, or empyema of the

opposite side. It may also be due to some complication outside the chest, the most common being otitis media. In all such cases a careful and complete physical examination should be made, and the urine should be examined for possible pyelitis.

The chief obstacle to a completely successful result in empyema is defective expansion of the lung. This is the condition found so frequently at autopsy in the many fatal cases in infancy. In older children this condition is less common, expansion taking place readily in cases operated on comparatively early. When insufficient, it may be promoted by the apparatus devised by James, which serves also as a toy for the child's amusement. Air is blown by the child through a tube into a corked bottle containing a colored fluid, and this forces the fluid out through another tube into a bottle placed at a higher level, the fluid flowing back by siphonage. Blowing soap bubbles, or a game in which a feather is blown about upon a large table, answers the same purpose. Such methods of promoting lung expansion cannot be employed in infants and very young children. The chief agent is the cough, and no medication tending to check cough should be employed after operation for empyema. It is advisable to change the child's position frequently, and an attack of crying is not to be suppressed, as it favors lung expansion.

In some cases, which through neglect, or injudicious delay in operating have become chronic, complete expansion of the lung is prevented by the firm fibrous adhesions which have formed. The chest wall recedes to its fullest extent, the ribs being in contact, but nevertheless a cavity may remain which cannot close. The existence of such a cavity prevents a cure of the suppurative process, and leads to a fatal ending. Such cases are rare; the only hope is the operation of thoroplasty, in which a greater collapse of the chest wall is permitted by the removal of portions of several ribs. The operation is serious, and is followed invariably by great deformity.

SEROUS PLEURISY

This form of pleurisy is much less common in children than in adults, and is seen most often in older children, being rare in infancy and early childhood.

ETIOLOGY.—Pleurisy with serous effusion may occur as a complication of pneumonia. It may also occur as does empyema in the course of any of the infectious diseases, the primary source of infection being a latent bronchopneumonia. In these cases, which are comparatively uncommon, the organisms causing the pleurisy are the same as those concerned in the etiology of empyema, the pneumococcus being the form most often seen, with the streptococcus next. The only difference between these cases and empyema is that the

exudate is sero-fibrinous instead of purulent. In the majority of cases of this type, the serous effusion represents merely a very early stage of a developing empyema, the fluid containing large numbers of the pus-producing microorganisms, and later becoming purulent. For all practical purposes these are cases of empyema. In a few cases, however, in which the pleural inflammation originates in a pneumonia, the exudate does not become purulent, the disease running a course resembling that of other etiologic types of serous pleurisy. In such cases the number of microorganisms in the fluid is usually small.

The commonest etiologic form of serous pleurisy is the tuberculous. This is rare in children under the age of seven years, but forms the majority of the cases of serous pleurisy encountered in later childhood. It represents invasion of the pleura by the direct extension of tubercle bacilli from the lung, either from the primary lesion or from a tuberculous bronchopneumonia.

Second in frequency as a cause of pleuritic exudate which remains serous throughout, is rheumatic fever infection, although pleurisy is one of the rarer manifestations of rheumatic fever. These cases either accompany or follow the rheumatic fever attack. It is probable that the occasional instances of pleurisy complicating tonsillitis are also etiologically manifestations of rheumatic fever. In rheumatic pleurisy the process may be bilateral. The fluid shows all the characteristics of a sero-fibrinous exudate, but is usually free from bacteria.

Pleurisy is sometimes associated with nephritis, but in the majority of cases, especially when the process is bilateral, the effusion represents a transudate rather than the inflammatory exudate of a true pleurisy.

PATHOLOGICAL ANATOMY.—The process is a typical sero-fibrinous inflammation. The surface of the pleura is covered with fibrin as in dry pleurisy, but, usually from the very beginning, serum is exuded from the blood-vessels. The quantity of fluid is very variable; it may form only a thin layer, or may fill the pleural cavity with marked compression of the lung. In cases of tuberculous or rheumatic fever origin, or of pneumonic origin not going on to pus formation, the fluid is of a clear, pale-yellow color, coagulates spontaneously, and contains flocculi of fibrin and a few leukocytes and endothelial cells. The amount of fibrin varies. A greater proportion of fibrin is likely to be present in the exudation in children than in adults. In cases in which the process represents the early stage of an empyema, the fluid is more cloudy, and contains more leukocytes and many bacteria.

The termination of the process is absorption of the exudate. Whenever the quantity of fibrin is considerable, not all is absorbed, but a certain amount of fibrous tissue organization occurs which produces thickening of the pleura, and fibrous adhesions of varying extent. The adhesions are not likely to interfere with expansion of the lung in serous pleurisy.

SYMPTOMS.—The cases occurring in connection with pneumonia in which the quantity of serous exudate is too small to reveal itself on physical examination, have no characteristic symptoms, and will not be described here. The symptoms of the cases which go on to pus formation are precisely like the symptoms of empyema which have been already described.

The onset of serous pleurisy may be acute, or it may be insidious. In the acute cases there is fever, cough, pain, and rapid breathing, and the onset resembles that of lobar pneumonia, except that all the symptoms are less severe. The fever is not so high, rapid breathing comes on more gradually, general constitutional disturbance is less, and such signs of nervous system intoxication as apathy or delirium are notably absent. On the other hand, cough is often more marked than in lobar pneumonia, and pain at the onset may be more severe, often being referred to the abdomen. The signs of fluid in the pleural cavity develop rapidly, and are usually marked before the end of three days. With the accumulation of the fluid the temperature often becomes lower with marked remissions, and there is a lessening of the severity of the cough and disappearance of the pain. On the other hand, the rate of respiration may become more rapid.

In the more insidious class of cases there is often little or no fever, cough is slight, and pain absent. There is general weakness, pallor, and moderate prostration, but the only symptom pointing toward the chest as the seat of disease is a gradually increasing shortness of breath. The severity of the symptoms is very variable. In some cases there may be no marked symptoms, the accumulation of fluid being only revealed by physical examination of the chest.

In the majority of cases the serous effusion, after accumulating for two or three days, remains at its maximum for three or four days more, and then begins to diminish in quantity. Absorption continues, but is less rapid than accumulation, and is usually completed in a week or ten days. In a few cases there is no tendency toward absorption, and the accumulated fluid remains indefinitely unless removed by aspiration. In this chronic stage there may be some fever, usually slight, and there is often increasing pallor, loss of strength, and loss of weight. The general symptoms in this stage are those of chronic tuberculosis.

In most cases the quantity of accumulated fluid is not sufficiently large to produce serious symptoms from pressure. Occasionally, however, when the fluid accumulates rapidly, pressure symptoms are seen, usually early in the course of the attack. There may be marked dyspnea or even orthopnea, cyanosis, and weak pulse. There may even be fainting attacks, and rarely pressure symptoms severe enough to cause death are seen.

The physical signs of fluid in the chest are the same whether the effusion be serous or purulent, and have been thoroughly described under empyema.

DIAGNOSIS.—The first step in diagnosis is to establish the presence of fluid in the pleural cavity. The differentiation between fluid and pulmonary consolidation has already been discussed under the diagnosis of empyema.

The presence of fluid having been established or suspected by means of the physical examination, the next step is to determine whether the fluid is serous or purulent. Serous fluid may be suspected in cases occurring in older children without obvious connection with pneumonia or other acute infection, in cases occurring in rheumatic fever patients, and in cases of insidious onset, without marked fever. An absence of leukocytosis is in favor of tuberculous pleurisy with serous effusion. Nevertheless, on a basis of the history and physical examination, the physician cannot do more than form a guess as to the nature of the effusion in cases of pleurisy. The final diagnosis rests upon the results of exploratory thoracentesis. As empyema is so much more common in early life than is serous pleurisy, the burden of proof lies on the diagnosis of the latter. It is extremely important for therapeutic purposes to obtain early proof of the presence of empyema. Consequently, exploratory puncture should be performed in every case in which the presence of fluid cannot be excluded.

If the fluid obtained by exploratory thoracentesis is serous, the next step in diagnosis is to determine as far as is possible the etiological nature of the pathological process. This is much aided by laboratory examination of the fluid obtained. The method of examining exudates and transudates is described in Division II, p. 134. The first step is to determine that the fluid is an exudate and not a transudate. An exudate is recognized by the high specific gravity (1.016-1.026), the high albumin content (2-6%), and the presence of fibrin and leukocytes. The diagnosis of the etiology of an exudate depends upon the results of cyto-diagnostic and bacteriological examination. In an exudate due to one of the organisms concerned in the production of an antecedent pneumonia, the predominating cell is the polymorphonuclear leukocyte, and the organism—pneu-

mococcus, streptococcus, staphylococcus—playing an etiologic rôle will be found in coverglass preparations. In exudates which represent an early stage of empyema, later becoming purulent, the fluid is usually slightly turbid, and both leukocytes and bacteria are numerous. In exudates due to pneumonic pleurisy which nevertheless later remain serous, the fluid is usually clear, leukocytes are less numerous, and bacteria are few. Nevertheless in every instance in which pus-producing organisms are found in the fluid, another exploratory puncture should be made in a day or two, in order that the development of empyema may not be overlooked. In cases in which the pleurisy is the result of tuberculous infection, there is an increase in the number of mononuclear cells (lymphocytosis), and the lymphocyte is often, but not always, the predominating cell. The ordinary bacteriological examination with Loeffler's methylene blue reveals no microorganisms, and cultures remain sterile. A positive diagnosis of tuberculous pleurisy can only be made when the special stain for the tubercle bacillus reveals the presence of that organism, but the demonstration of the tubercle bacillus in the pleuritic exudate is even more difficult than in the cerebrospinal fluid, and cannot usually be obtained. The presence of a positive von Pirquet cutaneous tuberculin test is very important in the diagnosis of tuberculous pleurisy. For prognostic and therapeutic purposes it is best to assume that every case of serous pleurisy having a sterile fluid and not connected with rheumatic fever, is of tuberculous origin. In the rare cases of serous pleurisy occurring as a manifestation of rheumatic fever, the fluid contains no microorganisms, but the predominating cell is the polymorphonuclear leukocyte. The diagnosis depends more upon the association of the pleurisy with other rheumatic fever symptoms, than upon the examination of the serous exudate.

PROGNOSIS.—The prognosis in typical cases of serous pleurisy is good. The only exception is the cases complicating pneumonia in which the effusion later becomes purulent, and in which the prognosis is that of empyema. The prognosis of tuberculous pleurisy is that of chronic tuberculosis at that age. Pleurisy is one of the most favorable secondary manifestations of tuberculosis, and tends strongly toward recovery. Moreover the occurrence of pleurisy as the only secondary manifestation of tuberculosis is an indication that the underlying chronic infection is in a stage when high resistance has developed in the patient, and the outlook for eventual complete recovery from the tuberculous infection is in this stage very good. The course of rheumatic fever pleurisy is favorable as far as the pleurisy is concerned, the prognosis being that of rheumatic fever in general.

TREATMENT.—The treatment of the acute stage of serous pleurisy is only symptomatic. The general routine of treatment adapted to any acute infection should be followed. The only symptoms commonly requiring treatment are pain and cough. Pain is relieved by counter-irritation such as is afforded by a mustard paste. In many cases an ice bag gives more relief than a counter-irritant application. At times a rather tight swathe about the chest will give more relief than anything else. If the pain or cough be very severe, some preparation of opium should be used, but this is rarely necessary in children. Cough is rarely severe enough to require medication.

The bowels should be kept properly open by means of mild saline cathartics, but ordinarily it is not well to try to hasten absorption by purgation, diuretics, or limitation of fluid intake. The exudate is of an inflammatory character, and will be absorbed spontaneously when the inflammation subsides. No drug has any specific action in hastening absorption, and the use of such drugs as iodid of potassium, falsely supposed to promote the absorption of exudates, only tends in childhood to disturb the digestive system.

When absorption is delayed and the disease tends to become chronic, the best method of treatment is the removal of a part of the fluid by aspiration. This procedure is usually quickly followed by spontaneous absorption of the remaining fluid, and as a means of treatment is far preferable to purgatives, diuretics, and limitation of fluid intake. The latter measures should only be used in case the effusion tends to reaccumulate after aspiration. When this occurs it is not wise to repeat aspiration more than once, on account of the danger of wounding the lung.

Aspiration is positively indicated in cases in which the accumulation is so rapid that serious pressure symptoms develop.

Patients with tuberculous pleurisy should receive the general dietetic and outdoor treatment which is employed in tuberculosis in general.

FIBRINOUS PLEURISY

A certain amount of fibrinous pleurisy is an almost invariable accompaniment of all forms of pneumonia, and cannot be considered as an independent clinical disease. In later childhood, are seen cases of fibrinous pleurisy which clinically appear to be primary.

ETIOLOGY.—It is probable that the cases are not really primary but that they have the same etiology as serous pleurisy. This means that the pleurisy is secondary, either to a small latent pneumonia, to tuberculosis, or to rheumatic fever. The exciting causes are the same as in serous pleurisy. Even in older children, dry pleurisy is much less common than in adults.

PATHOLOGICAL ANATOMY.—The pleura is injected and without luster. At first it is covered with a thin layer of lymph which becomes opaque and thickened by the deposition of fibrin and leukocytes. The sub-pleural fibrous tissue is also thickened by the exudation of serum and by cellular infiltration. The roughened surfaces of the visceral and parietal layers may adhere, forming loose connections which may subsequently undergo organization without producing an exudation and end in a chronic adhesive pleurisy. The areas of inflamed pleura may be large, or small and diffusely located. There may be an extensive layer of fibrin of variable thickness over the pleural surface. In tuberculous pleurisy there may be, in addition to the fibrin, tubercles or caseous nodules on the pleural surface and in the layers of the exudate.

In the further course of the process part of the exudate is absorbed. A certain amount is left behind, which undergoes fibrous tissue organization, the result being thickening of the pleura and adhesions. There is probably some thickening of the pleura after every case of fibrinous pleurisy. The thickening especially in tuberculous cases may be very pronounced and adhesions may be very extensive.

SYMPTOMS.—The symptoms of the pleurisy which regularly accompanies pneumonia are usually indistinguishable from those of the primary disease. Only the pleuritic friction rub is a distinctive evidence of the presence of pleurisy, and this is not always heard even in cases in which fibrinous exudate on the pleura is found post-mortem.

In cases which clinically appear to be an independent disease, the chief symptoms are pain and cough. The pain is sharp and stabbing, and is increased by cough or deep inspiration. It is usually sharply localized, but the localization often does not correspond to the seat of the lesion. The pain may be referred to the abdomen, or even to the side opposite to the one affected. The cough is short, and dry, and often has a peculiar sound suggesting that the child is making every effort to suppress it. There is usually little or no fever, and no constitutional symptoms.

On physical examination, the only abnormality, is the presence of a pleuritic friction sound. This is a dry rubbing sound, usually heard both with inspiration and expiration, and ordinarily sharply localized. The most common situation of the friction rub is the axillary region. The usual duration of this condition is from a few days to a week. At times, after the lapse of several days, a dry pleurisy may be superseded by a serous effusion.

DIAGNOSIS.—The diagnosis depends upon the finding of the friction rub. The etiologic diagnosis depends, upon the general history of the case. If there is a history of previous tuberculous manifestations, or if d'Espine's sign is present or the von Pirques

reaction positive, the evidence points toward a tuberculous etiology. If there is a history of rheumatic fever manifestations, the pleurisy is probably a manifestation of that infection. If the pleurisy is associated with exposure to cold, or with any recognizable acute infection, the cause of the process is probably a latent pneumonia.

PROGNOSIS.—The prognosis is good. In general, it resembles that of serous pleurisy, depending on the underlying etiology.

TREATMENT.—The treatment is the same as that described for the acute stage of serous pleurisy.

CHRONIC ADHESIVE PLEURISY

Chronic pleurisy results from previous attacks of acute inflammations of the pleura, either with or without the formation of fluid. The result is essentially the same differing chiefly in degree. The lesions are represented by adhesions between the thickened layers of parietal and visceral pleura. Large or small areas of the cavity may thus be obliterated. The physical signs are represented chiefly by dulness and diminution in the intensity of the breathing, voice-sounds, and tactile fremitus. Litten's phenomenon is absent. On the other hand, adhesions are often found at the autopsy, where during life both lungs seemed perfectly normal. The diagnosis is aided by the use of an aspirating needle, by which we can often determine by the sense of touch whether the needle is in a thickened pleura, the lung, or a free cavity. If the adhesions are extensive, retraction of the chest with certain compensatory changes occur.

TREATMENT.—The treatment consists entirely of general hygiene and systematic exercises of the chest.

INFLUENZA

The article on influenza in this volume (p. 237), was written before the recent pandemic of 1918-19 and 1919-20. This epidemic has thrown much new light on the nature of epidemic influenza, and has cast a doubt on many views which have been previously accepted. The disease may be defined as an acute epidemic infection affecting chiefly and primarily the respiratory tract. It is at present by no means clear just what relation the disease seen in the recent epidemic bears to that seen in the epidemic of 1889, and to the various non-epidemic infections of the respiratory tract which are often spoken of as influenza or grippe.

ETIOLOGY.—*The Microorganism.*—In spite of much investigation, the etiology of the disease seen in the recent epidemic is still unknown. The discussion has finally come down to the question whether or not the *Bacillus Influenzae* described by Pfeiffer after the

epidemic of 1889-90 is the cause. In favor of the Pfeiffer's bacillus as the cause is the frequency with which it is found in the secretions of the nose and throat in cases of influenza. On the other hand, the weight of the experimental evidence is against the Pfeiffer's bacillus as the primary cause. I have recently been over the literature, and have come to the conclusion that the probability is that epidemic influenza, at least as seen in the recent pandemic, is not caused by the Pfeiffer's bacillus, but by some other microorganism, as yet unknown.

Even if the *bacillus influenzae* is not the primary cause of the disease, there can be no doubt as to its importance as a secondary invader. Other organisms found in the same rôle are all four types of the pneumococcus, the streptococcus hemolyticus, the micrococcus catarrhalis, the staphylococcus aureus, the streptococcus viridans, and Friedlander's bacillus.

Transmission.—The manner of spreading of the recent pandemic is still unknown. It was assumed that the transmission of the disease was similar to that of measles and whooping-cough, that is, by droplet infection. Experimental work has thrown considerable doubt on this assumption. The peculiarly rapid spread of the disease in a community was more like that seen in a water or milk-borne epidemic, than in an air-borne contagion.

Predisposition.—It was stated early in the course of the epidemic that infants and young children were less susceptible to infection than adults. This impression came from the fact that the mortality among children is much lower than among young adults. There is no difference in susceptibility to infection, and the disease was common even in very young infants. During the height of the epidemic, practically all the beds at the Infants' Hospital, which admits patients only under two years of age, were occupied by influenza patients.

Incubation.—The period of incubation is very brief, and has been reported as from one to two days. It is established that the disease can develop in this brief period, but it has not been proved that the incubation period may not be longer.

PATHOLOGICAL ANATOMY.—The lesions show no modifications peculiar to early life.

SYMPTOMS.—The clinical course of the disease in early life does not present sufficient variation from that of adults to warrant detailed description. There is the same extreme rapidity of onset with high fever and marked prostration. The subjective symptoms such as pains, headache, and chills, are less frequent and marked in childhood, and as far as we can judge by observation, are usually absent in infancy and early childhood. A uniform drowsiness, which may even amount to stupor, is peculiarly characteristic of the dis-

case in early life. Loss of appetite is common and often extreme. Nausea and vomiting, and diarrhea are seen at times, but no more frequently than in adults. Cough and coryza are less marked than in adults.

Upon physical examination the only signs found in the majority of cases, beside the general evidences of acute infection and prostration, are reddening of the pharynx and conjunctivae. I believe it is important to distinguish the signs due to the uncomplicated specific influenzal infection of unknown etiology, from the signs due to complications caused by the secondary invaders. As a part of the primary infection, there may be evidences of rhinitis, pharyngitis, laryngitis, or tracheitis. When physical examination shows in the lungs signs of bronchitis or bronchopneumonia, I believe this is evidence of a complication produced by the invading microorganism. The signs of bronchopneumonia, in this epidemic, presented no features which could be called characteristic, or which differed from those seen in the bronchopneumonias complicating other acute infections in early life. Cyanosis is less commonly observed than in adults. Subcutaneous emphysema is no less common than in adults.

All the diagnostic laboratory tests are negative except the white blood count. There is some difference of opinion shown by the reports as to the leukopenia in early life. There is a tendency toward leukopenia in uncomplicated cases, but it is less constant than in adults. Even in pneumonia the white count is apt to be low.

The clinical course of the disease in early life shows no essential difference from that of adults. In uncomplicated cases the fever and other symptoms subside in a few days. In pneumonia, the course shows all the variations in severity and duration which are characteristic of the bronchopneumonias of early life.

COMPLICATIONS AND SEQUALAE.—Bronchopneumonia is the most important. It is considered by many authorities as a part of the disease, but I believe it to be a complication caused by secondary invaders, among which the *B. influenzae* is particularly important. It occurs in about 10 per cent. of the cases seen in childhood.

A great number of other complications have been reported, most of which depend upon the spread of invading organisms to various parts of the body. None of them is particularly characteristic of influenza, unless it be a severe laryngitis, resembling diphtheria, called by Regan "influenzal croup." It is notable that meningitis does not appear in the list of reported complications. Meningitis caused by the Pfeiffer's bacillus is not uncommon in early life, and the absence of any increase in the reported cases during the recent pandemic is a strong argument against the primary etiological role of the *B. influenzae*.

DIAGNOSIS.—This depends mainly on the existence of an epidemic of the disease. It would be particularly difficult in early life, were it not for the recognized presence of the disease in the community, because the symptom-complex of sudden onset, high fever, drowsiness, and prostration are seen in a number of acute infections, and the clinical features particularly characteristic of influenza are less marked in childhood.

PROGNOSIS.—This is undoubtedly better in children than in adults. There is however some difference of opinion shown by the reports. Locke believes the death rate is high under five years of age. In my experience while it was higher than in later childhood, it was no higher than one would expect in connection with the various factors influencing the progress of all acute infections in infancy. Wollstein reported that the series of pneumonia cases following influenza seen at the Babies Hospital in New York was far more severe and more highly fatal than any other group of pneumonia cases observed in the hospital over a similar period of time. This was not my experience at the Infants' Hospital, where the pneumonia following influenza showed nothing characteristic in symptoms, severity, and fatality. In general, in giving the prognosis in an individual case, the physician may give a favorable prognosis in an uncomplicated case in a healthy infant or young child. He may give the liability to pneumonia as about 10 per cent., and the mortality of complicating pneumonia as about 50 per cent. This prognosis must be modified with infants in poor physical condition.

TREATMENT.—*Prophylaxis.*—It is impossible to give directions as to prophylaxis in a disease in which the mode of transmission is unknown. Various elaborate measures, such as the wearing of masks, were devised on the assumption that the disease was spread by means of droplets from the respiratory tract. There is no properly controlled evidence of the value of these procedures, and I believe they may do harm in giving the public a false sense of security. Strict isolation and quarantine is impractical during a pandemic of this nature. I believe, however, that children should be kept away from all places where humanity is crowded together, such as theatres, street cars, etc. I cannot give an opinion at present on whether or not it is advisable to close the schools, and keep children out of the churches.

There is some evidence of the value of vaccination in the prevention both of the disease and its complications. Such vaccines are prepared from the various organisms recognized as secondary invaders, including the *B. influenzae*. Most of the experimental work giving evidence of value was not properly controlled. McCoy studied a preventive vaccine under careful control, and found that it neither prevented the disease, nor influenced the incidence of pneumonia.

Specific Therapy.—There is no specific treatment available as yet in combatting the disease. The use of vaccines, either in the early stage as a preventive of pneumonia, or therapeutically for the various types of developed pneumonia, has not given any conclusive evidence of value. Most of the experimental work was not properly controlled.

There can be no serum therapy directed against the primary infection, until the etiology has been definitely established. The serum of convalescents from influenzal pneumonia was tried in the treatment of influenza complicated by pneumonia. McGuire and Redden reported strikingly favorable results. It must be remembered that the disease presents such variations in clinical course at different times, that the results from one observer at one hospital must not be given too great significance. Lord, at the Massachusetts General Hospital, and Locke, at the Boston City Hospital, reported a small series of carefully controlled cases in which no favorable results were obtained.

When Type I. pneumococcus is found in the sputum in pneumonia, anti-pneumococcic serum may be tried.

General Treatment.—In children the general treatment is that of an acute infection of similar severity, as described on p. 243.

End of Volume II

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